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HALOWAX ACNE ("CABLE RASH")

A CUTANEOUS ERUPTION IN MARINE ELECTRICIANS DUE TO CERTAIN CHLORINATED NAPHTHALENES AND DIPHENYLS

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The present study is concerned with an eruption observed and studied in a series of marine electricians engaged in working with certain types of electrical cable in a large shipbuilding organization over a period of several years.

The first patient was seen on Dec. 31, 1941. The number of cases has gradually increased to a total of 52 at the time of writing. Many patients have been under constant observation for a period of one and one-half to two years. The studies on hepatic function to be described were based on a selected group of 25 patients who presented a more extensive involvement. New cases still are developing, and the study continues. A cooperative and free exchange of information with physicians elsewhere in the United States who are seeing and treating patients with this eruption has been maintained. This has been mutually helpful in the attempts to solve the problems presented and beneficial to the patients in the relief that it has been at times possible to afford them.

Halowax acne or "cable rash" is the general term commonly used to designate the eruption. It is by no means a new clinical entity. Soon after the introduction of tar and its derivatives into industry, acneform eruptions began to appear and were reported in the literature by early observers. Dermatologists and industrial physicians studied the causation, control and prevention intensively. Most of these studies have appeared in specialized publications, principally those devoted to industrial medicine.

Perna Krankheit was the term used to describe the condition by the German writers [1] at the time of World War I. This acneform eruption, identical with the clinical picture now appearing, occurred among workers on gas masks and on gas-proof clothing. It was caused by chlorinated naphthalenes.

Today chemically related substances (known by the trade name Halowax) are being used in considerable amounts on ships. Halowax is manufactured and compounded by the Halowax Corporation, a subsidiary of the Union Carbide and Carbon Company. It is a waxlike substance, a mixture of chlorinated hydrocarbons produced chemically by chlorination of naphthalene and diphenyl. This material is incorporated into electrical cables designed for specific purpose on naval vessels.

1. Teleky, L.: Die Pernakrankheit (Chloracne), Klin. Wchnschr. **6**:845 and 897, 1927. Koelsch, F., in Ullmann, K.; Oppenheim, M., and Rille, J. H.: Die Schädigungen der Haut durch Beruf und gewerbliche Arbeit, Leipzig, Leopold Voss, 1926, pp. 303-343.

It is a unique and invaluable material, possessing many essential and desirable qualities. Extremely resistant to physical wear, chemical corrosion (including sea water) and wide range of changes in temperature, it is, in addition, waterproof and ratproof. It strongly withstands heat and flame. Its value as an insulation for electrical currents is extremely high. Under heat it has a desirably high "flow point." By varying the degree of chlorination, materials of different plasticity may be obtained. The hardness of the Halowax is directly proportional to the percentage of chlorination. An average composition is 20 per cent pentachloronaphthalene and 80 per cent hexachloronaphthalene, to which as much as 20 per cent chlorinated diphenyl may be added. In such a mixture there may be a chlorine content of approximately 60 per cent. The content may be adjusted to as low as 30 per cent or as high as 80 per cent, depending on the physical characteristics desired.

Halowax is principally used in insulating wire for systems of intercommunication and for the de Gausse system of rendering ships electrically neutral to magnetic mines. When in operation, a constant electric current of high amperage is (constantly) passing through cables strung through the entire length of the hull of the boat. This current, acting as a "flux," effectively counteracts and neutralizes the electric currents generated by the myriad of electric apparatus, including generators aboard modern ships, and the steel of the boat as it travels through the water.

The cables themselves are relatively flexible. They are not too bulky or cumbersome (and occupy comparatively little space) and are designed to facilitate ease of installation and connection. They are metal covered. The approximate diameter is about 3 inches (7.5 cm.). The cable consists of individual bundles of copper wire. Each bundle is coated with Halowax impregnated into asbestos. The bundle is then coated with a layer of cellophane. Surrounding this is woven an outer layer of rubberized fabric. This layer, in turn, has a rayon cover. By incorporating several such bundles together, the large de Gausse cable itself is formed. Naval and cargo vessels are so wired.

In making electric connections and attaching lugs, the cable and individual bundles are "skinned." By "skinning" is meant the cutting back of the metallic outercovering and the individual covering of the bundles for several inches. The covering materials, including the Halowax, are removed and the bare copper strands exposed. In this process Halowax particles, in the form of a fine gray powder, are emitted. A dust is generated. At times it may be necessary to heat the cable and bundle ends to effect connections. In addition to the dust itself, the electricians are exposed to the fumes that may be generated by the heat. Because the wire is strung along the hull of the boat under construction, the spaces where the men work are necessarily close and confined. Ventilation is extremely difficult.

The acneform eruptions previously reported were observed among workers who, for the most part, were engaged in handling the chlorinated naphthalenes derived from crude tar (tar camphor, naphthalene, white tar naphthalene) ($C_{10}H_8$) in the preparation of the synthetic wax plasticizing materials, usually in a molten or hot state, or when the product thus obtained was melted and various kinds of electrical apparatus (such as condensers and coils) were dipped into it for securing insulation.

In the present cases the eruption observed was in electricians handling the cold-finished product for the most part. Only rarely was heat used, and the exposure to any fumes so generated was slight. The latest method of connecting the wire

practically eliminates the use of solder and heat. An ingenious lug is used that firmly and securely attaches the wire to the points desired purely by mechanical friction and pressure.

Admirable descriptions of the lesions seen have been those reported by the American writers Schwartz,[2] Mayers and Silverberg,[3] and Sulzberger [4] and the British writer Thelwell Jones.[5] Schwartz's detailed study and report published in 1936 clearly establishes his priority on this subject. It was the first to appear in the American literature. In his cases the rash was encountered both in workers handling the hot molten material, being thus exposed to the fumes, and in persons working with the cold electric wire and cable. Mayers and Silverberg's study was based on workers engaged in the manufacture of electrical condensers. Thelwell Jones [5] observed the eruptions appearing in workers handling the crude naphthalene (tar) as it was chemically processed for use in industry. In both reports high degrees of temperature were involved and the concentration of fumes that the workers were exposed to was relatively high as compared with the present series. These writers described a variety of lesions. Mayers and Silverberg conveniently classified them into three main groups: (1) acneform eruptions with pustules, papules and large comedos; (2) vesiculoerythematous eruptions usually observed in dermatitis venenata; (3) simple erythematous eruptions with pruritus.

The eruption to be described and with which the present study is concerned has been noted by these previous writers. With the onset of present world hostilities shipbuilding construction expanded enormously. Considerable amounts of Halowax began to be used, and Halowax acne or "cable rash" began to appear in various shipyards. As a result, renewed interest in the problem has arisen. Marine electricians began to consult physicians not only for the rash itself but because of the disability produced. Time vital for the production of critical material was lost, because skilled electricians were obliged to do other kinds of work and new, untrained workers taught to do the work. When other workers learned of the rash, they were deterred from handling the cable. With the increasing employment of women in defense industries the situation may be further complicated.

INCIDENCE

Practically all workers in the department handling such cable tended to acquire varying degrees of "cable rash." The onset dated from a preliminary latent period of a few weeks to several months. The elements of hot weather and perspiration seemed to be definite predisposing factors. Many workers engaged in the late fall or winter did not begin to acquire any considerable number of lesions or have symptoms until the following spring and summer. Individual differences as to texture and coloring of the skin produced no appreciable variations as to

2. Schwartz, L.: Dermatitis from Synthetic Resins and Waxes, Am. J. Pub. Health **26**:586, 1936; Skin Hazards in American Industry: Part II, Public Health Bulletin 229, United States Treasury Department, Public Health Service, 1936; An Outbreak of Halowax Acne ("Cable Rash") Among Electricians, J. A. M. A. **122**:158 (May 15) 1943.

3. Mayers, M. R., and Silverberg, M. G.: Skin Conditions Resulting from Exposure to Certain Chlorinated Hydrocarbons, J. Indust. Hyg. & Toxicol. **20**:244, 1938; Effect upon Skin Due to Exposure to Some Chlorinated Hydrocarbons, Indust. Bull. New York State Dept. Labor, August 1938, p. 361; Effect upon Skin Due to Exposure to Some Chlorinated Hydrocarbons, Indust. Bull., New York State Dept. Labor, September 1938, p. 425.

4. Sulzberger, M. B.; Rostenberg, A., Jr., and Sher, J. J.: Acneform Eruption, New York State J. Med. **34**:899, 1934.

5. Jones, A. T.: The Etiology of Acne with Special Reference to Acne of Occupational Origin, J. Indust. Hyg. & Toxicol. **23**:290, 1941.

susceptibility to the development of the eruption. Dry and oily complexions as well as diverse types of skins were included in the various nationalities included in the survey. All the workers were men. The age group extended from 18 to 63 years. In a few cases the workers' wives had a slight eruption resembling their husbands', probably from contact with work clothes and from laundering shirts and underwear.

Patch tests were of no value in anticipating persons predisposed to acquire "cable rash." This observation has been consistently reported by all previous writers.

DESCRIPTION OF THE CUTANEOUS LESIONS

In addition to the usual acuminate papules which result from the mechanical plugging of the hair follicles and the orifices of the sebaceous glands (folliculitis), which become secondarily infected to form pustules, furuncles and abscesses, a follicular hyperplasia of the sebaceous glands of the skin of the face occurs. Large black comedos appear in the follicular orifices as a result of the activity of the follicle. At times these cysts are large enough to suggest milia. These "comedo-like" lesions are found in almost countless numbers on the exposed portions of the body, especially on the face and forearms. In many cases less numerous similar lesions were found scattered on the arms, torso and legs. The most frequent sites where lesions were found on all patients and in greatest amounts were on the skin over the malar eminences, the circumorbital areas, the margins of the lobes of the ears and the mastoid regions. Frequently they extended into the hairline and into the scalp. The eyelids and lips were devoid of lesions. The skin of the nose was rarely affected and presented relatively few lesions. The dorsa of the fingers were frequently involved, as were the forearms.

SYMPTOMS

In addition to the lesions described, severe, persistent and at times almost intractable pruritus at the sites affected was a common complaint. The pruritus was most noticeable in those workers who had a superimposed or complicating dermatitis in addition to the purely acneform lesions. Occasionally it was severe enough to require use of a sedative to secure sleep. Heat and perspiration aggravated the symptoms. Burning and soreness of the eyes ("bloodshot") were a frequent complaint. Many of the men were engaged in electric work in close proximity to electric welders, and flashes from the oxyacetylene burners may have aggravated this symptom. There were considerable dust and metallic particles in the holds of the ships where the men were laying cable.

Lassitude was the next and most common complaint. It was felt that the long hours, often an average of ten a day, together with the time required in traveling to and from work contributed to the fatigue of the men. Also many workers had been recruited from ordinary peacetime positions, often sedentary, and were employed after short intensive training courses. Ventilation to an adequate degree was impossible.

Other symptoms occasionally noted were anorexia, nausea, headaches, vague abdominal pains, impotence, loss of weight, insomnia, alopecia and disturbance in taste. Jaundice was never observed.

During the survey widespread publicity in the press to a small series of fatalities in plants processing the cable occurred. This factor definitely increased the number and variety of complaints.

Fig. 1.—Halowax dermatitis.

UNIV. OF MICH.

SYSTEMIC INVOLVEMENT

A series of patients with extensive cutaneous involvement were studied for possible systemic effects. In addition to clinical examinations, including fluoroscopic study, tests for hepatic function and impairment were included. Complete hematologic studies were made. No evidence of any visceral effect was obtained that could be ascribed to exposure to the chlorinated naphthalene and diphenyls. Particular attention was given to the possibility of hepatic damage (atrophy) and anemia suggesting the aplastic variety. No relation with "cable rash" or with any internal disturbance was disovered.

DURATION OF THE ERUPTION

As long as many of the electricians continued working with Halowax cable, the eruption persisted and even extended in some instances. With the onset of colder weather, the institution of preventive measures described later and aggressive local therapy, many were able to continue at their work and a decided amelioration of symptoms was effected. The eruption itself was improved in many in this group. In a minority of the patients the eruption persisted for as long as one and one-half years after treatment and total freedom from exposure. These patients are still being observed.

THERAPY

In addition to prophylaxis many measures were used to relieve symptoms and improve the eruption. These included various keratolytic agents, such as sulfur and salicylic acid, and antiseptics, such as resorcinol, sulfonamide compounds, ammoniated mercury and ichthammol. These were used in various ointment and liquid bases. Emulsions of both oil in water and water in oil types were used. The ointment bases included those ordinarily used, together with several of the more recent types incorporating wetting agents. Various soaps containing substances conceivably indicated for controlling and improving the eruption were tried. Among these were proprietary "antiseptic" and "germicidal" soaps commonly found on the market; soaps containing pumice, marble and sulfur were also included. Various sulfonated oils were tried. Soaps containing trisodium metaphosphate were at times of value as detergents. Morris' recently suggested cleansing mixture incorporating oleic acid and butyl stearate has not had sufficient trial. A few related formulas were found of some value. Those consisted of 45 per cent sulfonated neat's foot oil, 45 per cent light liquid petrolatum and 10 per cent of a solution of gelatin (1 part of gelatin in 4 parts of water; 1 part of this preparation was added to 1½ parts of white granulated corn meal, with a trace of 0.5 per cent chlorobutanol as a preservative). Another detergent used consisted of sulfonated castor oil with a p_H of 7.2 and containing 50 per cent of oil content, together with 2 per cent of a wetting agent (aerosol OT dry, the dioctyl ester of sodium sulfosuccinate in 99 to 100 per cent concentration).

For patients with acute dermatitis wet compresses of commonly used medicaments were used to allay the symptoms. These included isotonic solution of sodium chloride, 3 per cent solution of boric acid, hot magnesium sulfate solution, solution of boric acid and salicylic acid (Thiersch's solution), and solution of aluminum acetate (Burow's solution) 1 : 20 to 1 : 10. Solution of sulfurated lime (Vleminckx' solution) in varying concentration was found ineffectual and irritating. Sodium hexametaphosphate in 1 per cent concentration seems to merit further trial.

Roentgen and ultraviolet therapy in careful dosages were of distinct value in relieving symptoms and accelerating the restoration of a clearer skin. Solid carbon

dioxide seemed occasionally beneficial. Attempts at removal of the hyperkerotic plugs by adhesive tape left on for varying periods were futile. Vaccines, autogenous and stock, had no demonstrable value. Mechanical removal of the plugs in the follicles by use of a comedo extractor or by facial massage was sometimes helpful. Osborne [6] called attention to the fact that the substances in the follicles are lipid solvents, fixed in the tissue by lipids. He suggested that a low fat diet would be of value in eliminating these substances and possibly as a preventive measure. Unfortunately, there has not been the opportunity for pursuing these studies.

PROPHYLACTIC MEASURES

In order to prevent the development of "cable rash" and ameliorate the symptoms in persons already affected, no expense was spared. Determined efforts to reduce the concentration of Halowax in the workers' environment were made. At the same time measures to promote rigid cleanliness of the skin were instituted. These preventive measures included ventilating by blower and exhaust fans, frequent change of clothing, both work clothes and underwear, individual lockers and adequate facilities for securing and opportunities to secure a thorough cleaning of the skin during the work day. Frequent changes of clothing were stressed; hot water was provided, and the employees were given an opportunity to wash and take shower baths on the company's time. Coverall work uniforms were provided. Various protective creams were furnished to the workers, and they were instructed in detail as to how and when to use them. These creams were used alone or with some of the soaps recommended with them. The sulfonated oils aforementioned were used as substitutes for soap. The value of such creams has not been adequately demonstrated as a preventive measure as yet. Use of coveralls and other protective clothing devices, such as face masks, sleeves and trousers, is being continued. It has been found that they increase the amount of heat and perspiration and that the workers do not cooperate in using them. They seem also to aggravate the condition. Large doses of the entire vitamin B complex, a liberal intake of carbohydrate, adequate intake of fluids and ingestion of saline tablets to combat loss of salts were found to be of value in controlling symptoms due to fatigue. The excessive use of alcohol and tobacco was discouraged.

One possible means of attack of the problem is the ingenious suggestion of Sulzberger. This involves the discovery of some chemical neutralizer against the Halowax that could be applied to the skin of the workers before and during their work with the cable. Such a substance might be incorporated in one of the new "penetrasols" he and his co-workers [7] have developed. Such "penetrasols" have been demonstrated to possess considerable powers of penetration into the hair follicles and ducts of the glands situated in the skin. This property is due to the wetting agents and fat solvents contained in them. If after a reasonable period no improvement was obtained, the worker was transferred to an entirely different position.

MECHANISM OF PRODUCTION OF LESIONS

Because of the high incidence of Halowax dermatitis among a relatively large group of persons, the negative results of patch tests and the absence of acute vesicular dermatitis as seen in contact irritations at the site of exposure, it seemed unnecessary to assume a development of hypersensitivity to the wax. Rather, a

6. Osborne, E. D.: Personal communication to the authors.

7. Hermann, F.; Sulzberger, M. B., and Baer, R. L.: New Penetrating Vehicles and Lotions, Science **92**:451 (Nov. 13) 1942.

primary irritation by the wax was believed to be the method of production. The explanation of this eruption offered by other investigators seems to be adequate and borne out by the elements involved being a foreign body reaction in the hair follicles and sebaceous glands due to the presence of these chlorinated naphthalenes. This occurs from mechanical plugging by the particles per se and from the condensation of the fumes emitted by the waxes in the cable. Rubbing, scratching, perspiration and heat in the closed holds of ships were further predisposing factors. Schwartz and Tulipan stated that the fumes are not decomposed nor do they contain any free chlorine. They agree with other investigators that the chlorine radical itself has an irritating effect on the plugged follicle.

SUMMARY AND CONCLUSIONS

Synthetic wax (Halowax) dermatitis is a common cutaneous hazard in marine electricians handling certain types of electrical cables.

An increasing number of employees with this dermatitis may be anticipated in the near future unless suitable and adequate substitutes for these synthetic waxes are discovered or more effective means of prevention and therapy are developed.

An evaluation of various preventive measures is made.

The probable mechanism of the production of these lesions is discussed.

The absence of systemic, visceral and hemopoietic involvement in handling the "cold" dry synthetic wax cable is noted.

The chronicity of the eruption and its resistance to therapy are emphasized.

No evidence of internal absorption has been found in these cases

The cooperation of the following persons made this study possible: Col. L. Schwartz, United States Public Health Service, and Drs. J. J. Brozdowski, J. Herradora, A. G. Cranch, J. A. Hookey, E. D. Osborne, G. E. Morris and M. B. Sulzberger.

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CUTANEOUS TESTS WITH HEN'S EGG WHITE FRACTIONS IN ATOPIC INFANTILE ECZEMA

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Hill [1] in his classification of infantile eczema listed the following types: (1) atopic dermatitis, (2) seborrheic dermatitis, (3) contact dermatitis, (4) eczematous fungous infections and (5) erythroderma desquamativum (Leiner's disease).

Although we have seen all these eruptions in infants it has been our clinical impression that infantile eczema is of the atopic type in about 90 per cent of the cases. It is true that seborrhea may be associated with and even mask atopic dermatitis, but through careful study the role of atopy becomes apparent. It is here that the determination of causative factors and their removal are most likely to yield gratifying results—vast improvement or even complete cure. The following accepted criteria of atopy are commonly well fulfilled in these cases:

1. A family history of atopy (hay fever, asthma, infantile eczema).
2. Absence of a personal history of other atopic disturbances, since the infantile eczema is the first manifestation of atopy to make its appearance.
3. The presence of Prausnitz-Küstner passive transfer antibodies.
4. Reactions with immediate wheals to cutaneous tests with the usual protein atopens.
5. Eosinophilia.
6. Later development in many patients of other manifestations of atopy, such as hay fever and bronchial asthma.

Although infantile eczema is frequently an atopic disease, we have not found it necessary to perform cutaneous tests on these patients, since we usually have found that empiric elimination yields excellent results (Hill,[2] Sulzberger [3] and Rappaport and Hecht [4]). It is a well known fact that children with eczema react positively in most instances to cutaneous tests made with egg white. György, Moro

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1. Hill, L. W.: Eczema, in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1937, vol. 4, chap. 43.

2. Hill, L. W.: The Pharmacopeia and the Physician: The Treatment of Infantile Eczema from the Viewpoint of the Pediatrician, J. A. M. A. **111**:2113 (Dec. 3) 1938.

3. Sulzberger, M. B.: The Pharmacopeia and the Physician: The Treatment of Infantile Eczema from the Viewpoint of the Dermatologist, J. A. M. A. **112**:38 (Jan. 7) 1939.

4. Rappaport, B. Z., and Hecht, R.: The Pharmacopeia and the Physician: The Treatment of Infantile Eczema from the Point of View of the Allergist, J. A. M. A. **112**:317 (Jan. 28) 1939.

and Witebsky,[5] Moro,[6] Hill and Sulzberger [7] and Woringer [8] have called attention to this reaction, but its significance has been an enigma to pediatricians and allergists. It is well known that while most of these children react positively to cutaneous tests with egg white, many of them are not clinically sensitive to this substance. It is a fact that the reaction to egg white can practically be used as an indicator for the presence of atopy in infants. The latter diagnosis is frequently questioned when a reaction to egg white is not present.

It seemed possible that an explanation for the underlying abnormality in atopy might be discovered by means of an investigation of the significance of the reaction to egg white in infants. Furthermore, it was hoped that an explanation for the development of atopy from infancy to maturity might be obtained (Sulzberger and Hill [7]).

Schloss and his associates [9] initiated the study of the fundamental questions involved in the problem of atopy, using among other things the sensitivity to egg white in infants as a means to this end. Subsequently, the investigations of Moro,[6] Woringer [8] and others have also stimulated research in this direction. In an early investigation on anaphylaxis, Rosenau and Anderson [10] demonstrated that this form of sensitivity in the guinea pig was transmissible from mother to offspring in utero via the placenta. Subsequent investigations by Ratner and others [11] have established this fact. It has been frequently postulated that the development of atopic sensitivity in man is dependent on placental transmission. It was argued that the proteins of egg white passed the placental barrier and sensitized the fetus in utero. Donnally [12] expressed the opinion that the proteins of egg white were transmitted to the suckling child by way of the mother's milk, and a rather heated

5. György, P.; Moro, E., and Witebsky, E.: Eiklarempfindlichkeit bei Eczema infantum, Klin. Wchnschr. **9**:1012, 1930; Weitere Beobachtung über trophallergische Hautempfindlichkeit in frühen Kindesalter, ibid. **9**:1435, 1930.

6. Moro, E.: Ekzema infantum und Dermatitis seborrhoides; Klinik und Pathogenese, Berlin, Julius Springer, 1932.

7. Hill, L. W., and Sulzberger, M. B.: Evolution of Atopic Dermatitis, Arch. Dermat. & Syph. **32**:451 (Sept.) 1935.

8. Woringer, P.: Le diagnostic de l'eczéma du nourrisson, Rev. franç. de pédiat. **13**:117, 1937; Recherches sur l'origine de l'allergie du nourrisson, ibid. **11**:283, 1935; Sur les rapports de l'eczema avec l'allergie chez le nourrisson, ibid. **11**:409, 1935; Etude comparative de la valeur antigénétique de blancs d'oeuf de différentes provenances, Compt. rend. Soc. de biol. **115**:389, 1934; Effet de la vaccination B. C. G. sur l'allergie ovalbuminique du nourrisson, Bull. Soc. franç. de dermat. et syph. **41**:241, 1934; Recherches sur la désensibilisation specifique dans l'allergie ovalbuminique du nourrisson, ibid. **40**:509, 1933.

9. DuBois, R. O.; Schloss, O. M., and Anderson, A. F.: The Development of Cutaneous Hypersensitiveness Following the Intestinal Absorption of Antigenic Protein by Normal Infants, Proc. Soc. Exper. Biol. & Med. **23**:176, 1926. Anderson, A. F.; Schloss, O. M., and Myers, F.: The Intestinal Absorption of Antigenic Protein by Normal Infants, ibid. **23**:180, 1925. Lippard, V. W.; Schloss, O. M., and Johnson, P. A.: Immune Reactions Induced in Infants by Intestinal Absorption of Incompletely Digested Cow's Milk Protein, Am. J. Dis. Child. **51**:562 (March) 1936. Schloss, O. M.: The Intestinal Absorption of Antigenic Protein, in Harvey Lectures, 1924-1925, Philadelphia, J. B. Lippincott Company, 1925, p. 156.

10. Rosenau, M. J., and Anderson, J. F.: Anaphylaxis, in Harvey Lectures, 1908-1909, Philadelphia, J. B. Lippincott Company, 1909, p. 117. Anderson, A. F.: Transmission of Resistance to Diphtheria Toxin by the Female Guinea Pig to Her Young, J. M. Research **15**:241, 1906; Simultaneous Transmission of Resistance to Diphtheria Toxin and Hypersusceptibility to Horse Serum by the Female Guinea Pig to Her Young, ibid. **15**:259, 1906.

11. Ratner, B.: Allergy in Childhood: Modes of Acquisition, J. Pediat. **12**:730, 1938; Allergy in Childhood: III. Its Onset and Natural Progress, J. A. M. A. **111**:2345 (Dec. 24) 1938. Ratner, B.; Jackson, H. C., and Gruehl, H. L.: Transmission of Protein Hypersensitiveness from Mother to Offspring, J. Immunol. **14**:249, 267, 275, 291 and 303, 1927.

12. Donnally, H. H.: The Question of the Elimination of Foreign Protein (Egg-White) in Woman's Milk, J. Immunol. **19**:15, 1930.

controversy has raged regarding this possibility. Smyth and Bain [13] stated that they had proved that such transmission was impossible. Recently Brunner and Baron [14] reinvestigated the gastrointestinal absorption of undenatured protein in nursing mothers and were able to confirm Donnally's original observations. They expressed the opinion that sensitization to proteins is acquired in postnatal life and that transmission through mother's and cow's milk is an important source of atopens. Sulzberger and Baer [15] in a recent study performed tests with primarily urticariogenic substances on newborn infants and demonstrated the fact that their skin was at once capable of whealing. They suggested that the fact that atopic infants give no cutaneous reactions to any of the common allergenic excitants is not due to the inability of the infantile skin to wheal, but rather to absence of intrauterine sensitization to any of these allergens. They expressed the opinion that the atopic cutaneous sensitization is acquired during postnatal life on the basis of an inherited predisposition to specific sensitizations. The controversy is as yet unsettled.

Hektoen and Cole [16] in various publications have reported their studies on the chemistry and immunology of fractions of egg white. They isolated the following components: ovalbumin, ovomucin, ovomucoid and conalbumin. The conalbumin in egg white corresponds to the serum albumin fraction in chicken serum. The other components are specific egg white proteins possessing characteristic chemical, physical and immunologic properties. Cole was able to show that ovomucoid is not rendered insoluble or altered immunologically by boiling, whereas the other fractions are so altered. One of us (R. H.) in unpublished experiments performed some years ago found that patients who gave cutaneous reactions to tests with egg white might react to one or more of the various fractions but that ovomucoid elicited by far the greatest number of reactions, there being few if any persons sensitive to egg white who were not sensitive to this component.

It has been argued that sensitization to egg white, if it occurs via the placenta, would probably depend in great part on a noncoagulable fraction, since coagulated egg white would lose its characteristics during the process of digestion and would not reach the placenta in a form capable of stimulating immunologic processes. The uncoagulable portion could, however, reach the placenta and be passed over to the infant. The same holds true for sensitization by means of mother's milk as well as for sensitization by means of ingested egg white. The uncoagulable ovomucoid would most likely escape denaturation by cooking and digestion and pass into the circulation.

EXPERIMENTAL DATA AND COMMENT

We felt that one method of demonstrating the correctness of the foregoing theories would be by performing cutaneous skin tests on children with atopic dermatitis with the different egg white fractions previously described. All the children were examined by a competent allergist and dermatologist, and it was decided that each was definitely atopic.

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13. Smyth, F. S., and Bain, K.: Enteral Absorption of the Antigen and the Apparent Failure of Antigen Secretion in Human Milk, J. Allergy **2**:282, 1931.

14. Brunner, M., and Baron, B.: The Presence of Ingested Cottonseed Protein in Woman's Milk, J. Allergy **13**:359, 1942.

15. Sulzberger, M. B., and Baer, R. L.: Whealing Capacity of Skin of Newborn or Young Infant: Report of Experiments, Arch. Dermat. & Syph. **41**:1029 (June) 1940.

16. Hektoen, L., and Cole, A. G.: Proteins of Egg-White: Proteins in Egg-White and Their Relationship to Blood Proteins of Domestic Fowl as Determined by Precipitin Reaction, J. Infect. Dis. **42**:1, 1928.

We studied 46 infants with typical atopic dermatitis at the Children's Division of the Cook County Hospital. Of these patients, 24 were less than 1 year of age and 22 were more than 1 year of age. Twenty-two children with other dermatoses were chosen as controls. These included patients with seborrheic dermatitis, contact dermatitis, infectious eczematoid dermatitis, lichen urticatus and erythema multiforme.

The materials used in this study included purified fractions of ovalbumin, ovomucoid and ovomucin prepared from egg white, and conalbumin prepared from chicken blood. In addition, fresh and dried egg white and an extract of chicken feathers were also used. Twentieth-normal solution of sodium hydroxide was used as the diluent. All the scratch tests were performed with a Broadbent scarifier.

EVALUATION OF RESULTS

We found that 41 patients of 46 reacted to the ovomucoid fractions. Of the patients sensitive to ovomucoid 37 reacted to dried egg white, 39 to fresh egg white, 21 to ovalbumin, 17 to chicken feathers, 14 to conalbumin and 8 to ovomucin (1 of these patients was not tested with ovomucin).

Of the 5 remaining patients, 3 gave plus-minus reactions to ovomucoid and 2 gave no reactions. Plus-minus reactions were considered negative. In these 5 patients there were 3 definite positive reactions to dried egg white, and 1 plus-minus and 1 negative. There was 1 definite positive reaction to fresh egg white, and 1 plus-minus and 3 negative. There was 1 positive reaction to ovalbumin and 4 negative. Reactions to feathers were completely negative. There was 1 positive reaction to conalbumin and 4 negative. There was 1 positive reaction to ovomucin and 3 negative. One patient was not tested with this material.

When the results are evaluated from the point of view of incidence of positive reactions it will be seen that in the series of 46 cases there were 41 positive reactions to ovomucoid, 40 to dried egg white, 40 to fresh egg white, 22 to ovalbumin, 17 to chicken feathers, 15 to conalbumin and 9 to ovomucin. Two patients were not tested with the last-mentioned substance. The children used as controls did not react to any of the extracts.

CONCLUSIONS

We believe that even from this small series of cases one can draw the following inferences:

1. It is possible that the acquisition of sensitivity is dependent on the solubility of the atopen and its resistance to denaturation.

2. Since ovomucoid is the most resistant to heat of the fractions of egg white, one might expect it to be responsible for the greatest number of positive reactions to cutaneous tests with egg white in infants and young children with atopic dermatitis. Ovomucoid may then induce sensitization to the other fractions. However, sensitization to them may be subject to their specific chemical and physical properties.

3. Our observations confirm the clinical fact that sensitization to egg white does not necessarily carry with it sensitization to chicken feathers or serum, but a relatively high percentage of patients who react to cutaneous tests with egg white are also sensitive to tests with chicken feathers and a component of chicken serum (in our series the figures were 41.4 per cent and 34.1 per cent, respectively).

4. For the patients tested, positive reactions to cutaneous tests with egg white were not necessarily associated with clinical sensitivity, since only 6 subjects in this series had proved clinical sensitivity to egg white. The others were being exposed to egg white without apparent harm.

COLLOID PSEUDOMILIUM

REVIEW OF ITS NOMENCLATURE AND REPORT OF A CASE

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Wagner,[1] of Leipzig, in 1866 described the first reported example of colloid pseudomilium and called it "the colloid-milium of the skin." His patient was a healthy 54 year old woman with lesions across the forehead and on the upper portions of the cheeks and the bridge of the nose. The skin in these regions was thickened, hyperpigmented, furrowed and covered with numerous closely set millet grain–sized, round and oval, discrete papules. These looked, he said, exactly like vesicles, but differed from them in being distinctly solid (*auffallend derb*), so that it was impossible to rupture them with either finger tip or finger nail; moreover, when pricked with a needle they yielded no fluid except a drop of blood. By firm lateral pressure with a finger nail he was able to evacuate from the lesions little round or sausage-shaped masses of transparent whitish or pale yellowish material "like firm colloid." Like "the usual colloid," he said, this material was not altered by acetic acid, alkalis or sulfuryl iodide.

Histologic sections were not made, but from the microscopic examination of the extruded masses Wagner concluded that they must have been formed in the distal portions of the acini of the sebaceous glands and that they should therefore be called milium, or, to distinguish them from ordinary sebaceous retention lesions, "colloid-milium."

Besnier and Balzer[2] in 1879 showed that Wagner was wrong in supposing the sebaceous glands to be the site of origin of the colloid. Besnier proposed the name miliary colloidoma, but the designation offered by Balzer—*dégénérescence colloïde du derme*—in its English translation, colloid degeneration of the skin, has been the most widely used name for the disease and is the one employed in the Standard Nomenclature of Disease.

There have been occasional objections. Vidal and Leloir [3] and Auspitz [4] used the name "hyaloma" in order to avoid the rather vague and to them unsatisfactory term "colloid." The word colloid was good enough, however, for as careful an observer as Paul Unna [5]; and it has been made amply clear by Jager,[6] Reuter and Becker,[7] and many others, that "hyalin" is not a whit more precise or satisfactory a word than "colloid." Casazza [8] in 1937 and Fidanza [9] in 1939 retired with unneces-

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Read at the staff meeting of The Clinic, Honolulu, Jan. 9, 1943.

1. Wagner, E.: Colloid-Milium of the Skin, Arch. d. Heilk. **7**:463, 1866.
2. Balzer, E., cited by Unna,[5] Jager,[6] and Reuter and Becker.[7]
3. Vidal and Leloir, cited by Stelwagon, H.: A Treatise on Diseases of the Skin, Philadelphia, W. B. Saunders Company, 1910, pp. 660-662.
4. Auspitz, cited by Stelwagon, H.: A Treatise on Diseases of the Skin, Philadelphia, W. B. Saunders Company, 1910, pp. 660-662.
5. Unna, P. G.: The Histopathology of the Diseases of the Skin, New York, The Macmillan Company, 1896, pp. 976-991.
6. Jager, T.: So-Called Colloid Degeneration of the Skin, Arch. Dermat. & Syph. **12**:629 (Nov.) 1925.
7. Reuter, M. J., and Becker, S. W.: Colloid Degeneration (Collagen Degeneration) of the Skin, Arch. Dermat. & Syph. **46**:695 (Nov.) 1942.

(Footnotes continued on next page)

sary care behind the word "pseudocolloid"; but in general, opposition to the term "colloid" has disappeared and it is now generally agreed that the word is as exact a one as our present state of knowledge of the biochemistry of such substances will permit.

It is unfortunate, however, that Wagner's term "milium" was so hastily abandoned in favor of Balzer's "degeneration of the skin." Besides being unwieldly, this name has the serious fault of failing to convey anything of the appearance of the eruption. The word milium immediately suggests a small, round or oval, firm, light-colored, sharply elevated, indolent, invariably discrete papule, usually on the forehead or cheeks—precisely the outstanding physical characteristics of the usual lesion of this disease. Despite the fact that Wagner chose it for a wrong reason, it was admirably descriptive. "Degeneration of the skin" was not an adequate substitute for it, and it still is not, even though it has been copied from one American textbook of dermatology to another for the last thirty years. In Jadassohn's text [10] the expression "miliary colloid degeneration" is used, with the French alternative, *pseudo-milium colloïdale*. Both of these terms include the desirable reference to the physical form of the lesions; and the latter—in English, colloid pseudomilium—is so concise, so descriptive and so reminiscent of Wagner's original term that it seems by all odds the most generally suitable designation for the disease.

This term, colloid pseudomilium, appears to have been first used by Ramos e Silva [11] in 1933 and in an extensive review and case report by Monacelli [12] in 1934; it has since been used in at least two other reports by three other authors.[13] It is a designation which could not have been properly employed for the eruption in the cases described by Labadie,[14] Mook,[15] Oliver and Gold [16] or Reuter and Becker,[7] for example. In their cases the degenerative process may have produced the same "colloid" as that found in the lesions of this disease; and for their cases the name colloid degeneration of the skin is therefore perhaps a suitable one; but the depth and relative diffuseness of the process, and in Labadie's and Oliver and Gold's cases, the fact that only a single lesion was present, make it plain that these cases are not examples of the disease described by Wagner. The great majority of reported cases, however, have been of exactly the same type as Wagner's; and "colloid pseudomilium" would have been a proper designation for all of these, as it would for the characteristic case reported herewith.

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8. Casazza, R.: Pseudocolloid Milia and Tumors, Arch. ital. di dermat., sif. **13**:582 (July) 1937.

9. Fidanza, E. P.: Pseudocolloid Milium, Rev. argent. dermatosif. **23**:62, 1939.

10. Jadassohn, J.: Dermatologie, Vienna, Weidmann & Co., 1938, p. 283.

11. Ramos e Silva, J., and Fialho, A.: Colloid Pseudomilium, Rev. med.-cir. do Brasil **41**:11 (Jan.) 1933.

12. Monacelli, M.: Colloid Pseudomilium, Ann. de dermat. et syph. **5**:29 (Jan.) 1934.

13. Strada, F., and Rodeiro, M.: Colloid Pseudomilium, Rev. méd. de Córdoba **29**:621 (Nov.) 1941. Arguello, R. A., and Strada, F.: Colloid Pseudomilium, Semana méd. **1**:276 (Jan. 30) 1941.

14. Labadie, J. H.: Colloid Degeneration of the Skin, Arch. Dermat. & Syph. **16**:156 (Aug.) 1927.

15. Mook, W. H.: A Case of Colloid Degeneration of the Skin, Arch. Dermat. & Syph. **11**:709 (May) 1925.

16. Oliver, E. A., and Gold, M. A.: A Case for Diagnosis, Arch. Dermat. & Syph. **44**:302 (Aug.) 1941.

It seems likely that the confusion over nomenclature accounts for much of the confusion which exists regarding the number of "acceptable" cases of this disease which have appeared in the literature. Jager [6] in 1925 found 19 cases which he was able to accept as authentic. Labadie [14] in 1926 followed his lead with a list of 20. Fukai [17] in 1928 listed only 14 acceptable examples; he omitted 9 of Jager's cases and added only 1 case. Monacelli [12] in 1934 listed only 20 authentic examples (excluding, for example, Labadie's case). Reuter and Becker [7] in 1942 found 25 cases reported since Jager's review of the literature but were able to accept a total of "about 50" cases in all, 6 more than Jager would have allowed, and (up to 1934) 8 more than Monacelli had approved. Not included in Reuter and

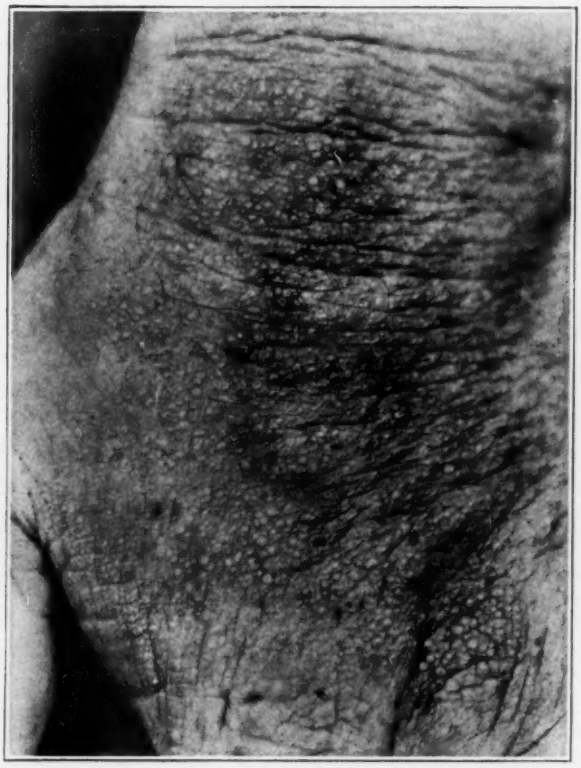

Fig. 1.—The back of the patient's left hand. Note the loss of elasticity and deep transverse furrows, the fading out of lesions over the wrist and knuckles and the discrete, shiny, translucent-looking, occasionally umbilicated elevations.

Becker's tabulation were 4 typical instances of the disease reported from South America [18] and 1 from Portugal.[19]

For a consideration of other aspects of this disease, the best articles are those of Monacelli [12] and Reuter and Becker.[7] In regard to treatment, Way [20] seems to have offered the most promising lead.

17. Fukai, A.: Colloid Milium, Acta dermat. **11**:155 (Feb.) 1928.

18. Fidanza.[9] Ramos e Silva and Fialho.[11] Strada and Rodeiro.[13]

19. Lapa, A., and Ferreira, C.: Colloid Milium, Lisboa méd. **8**:617 (Sept.) 1931.

20. Way, S. C.: Colloid Milium: A Vitamin Deficiency Disease? Arch. Dermat. & Syph. **45**:1148 (June) 1942.

REPORT OF CASE

K. C., a 42 year old Korean pineapple field overseer who had been employed outdoors constantly since coming to Hawaii from Korea at the age of 15, was first seen in November 1942, because of an eruption limited to the backs of the hands. It had been present for about

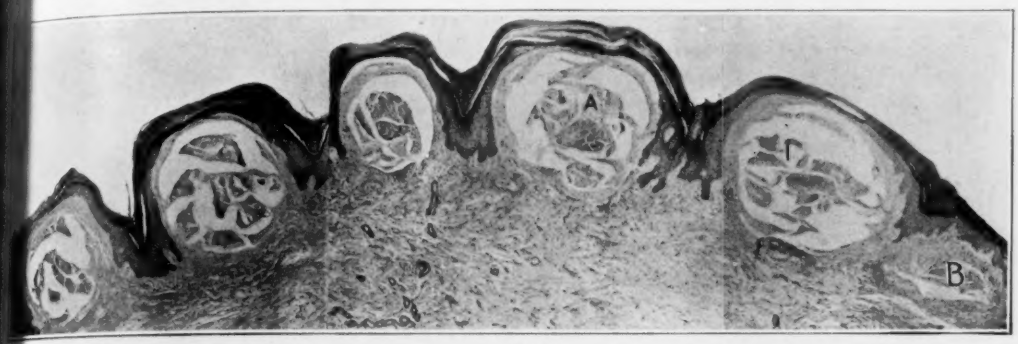

Fig. 2.—Photomicrograph showing four mature lesions, one nearly mature and one incipient lesion. Note the hyperkeratosis, the preservation of a band of collagen representing the obliterated dermal papillae, the shrinkage of the colloid "blocks" (artefact?), the fragmentation of the "blocks" (not artefact: Wagner [1] described this in freshly extruded material) and the presence of two lone vessels in one of the "blocks" (at *A*). Hematoxylin and eosin (× 17).

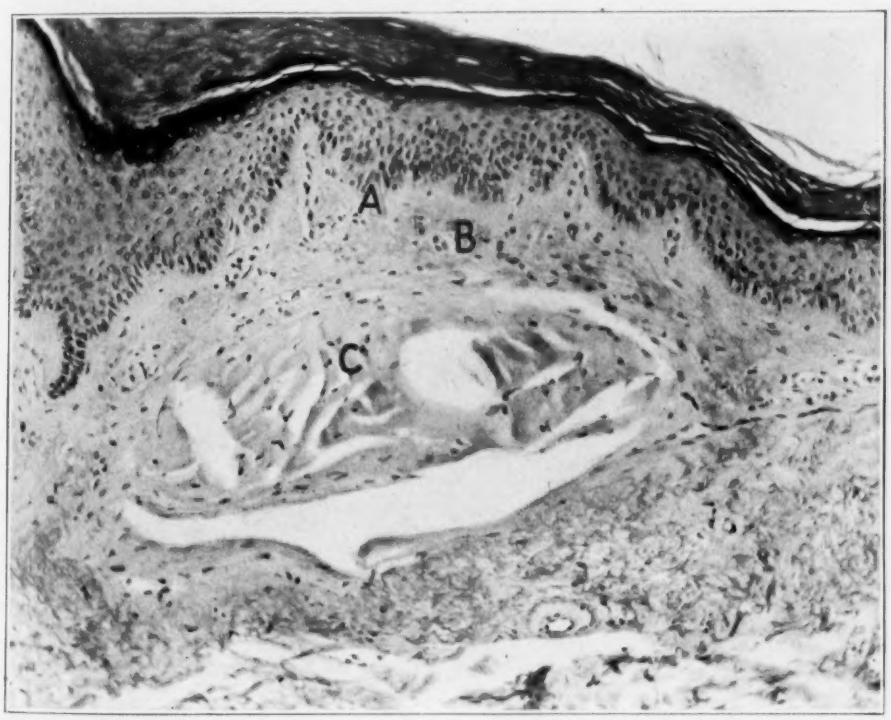

Fig. 3.—The incipient colloid "block" shown at *B* in figure 2. The epidermis is not remarkable except for hyperkeratosis. Note the relatively normal collagen in the papillary layer (*A*); the coarser feltwork of basophilic degenerated collagen at *B*; the colloid (*C*) and beneath it the feltwork of mingled fine and coarse fibers of degenerated connective tissue. Hematoxylin and eosin (× 130).

ten years on the right hand, and for a somewhat shorter period on the left. It had long since stopped spreading, and it had never given rise to any subjective symptoms. It was annoying to him merely because it looked and felt rough.

Examination disclosed a healthy, athletic-looking Korean man whose face and neck were deeply tanned except where a hat had shielded his forehead; the skin of these areas was perfectly smooth, however, and neither thickened nor atrophic. The backs of his hands were also rather tanned, and over them the skin looked and felt thickened and inelastic; it was deeply furrowed in a transverse direction, and was thickly covered with closely set but absolutely discrete, hard, sharply elevated, round or oval, flat-topped or slightly umbilicated,

Fig. 4.—A section just outside the region shown in figure 2. Normal collagen, in the papillary and deep portions (*B*) of the corium, is deeply stained; degenerated connective tissue and ill defined masses of colloid (*A*) are faintly stained. Note the fragmentation of the collagen fibers. Mallory's aniline blue (× 130).

translucent-looking papules from about 0.5 to 2 mm. in diameter (fig. 1). The lesions faded out rather abruptly on the wrists and the metacarpophalangeal joints.

Biopsy revealed (fig. 2) numerous nearly round spaces in the papillary and subpapillary layers of the corium, each incompletely filled by a fissured mass of about the same shape, consisting of homogeneous-looking material and several nuclei. In some of the masses, especially with certain stains, the nearly straight edges of some of the fragments seemed outlined by

fibrillar material. In one of the masses two small vessels were observed; in the others there was none. The epidermis over the masses was sharply elevated, and it was generally hyperkeratotic but otherwise unaltered. The collagen presented the general appearance of senile degeneration (fig. 3), fragmentation and hyalinization and basophilia in the subpapillary layer, not abnormal perhaps in a man who had worked out of doors daily, in sunny portions of an exceptionally sunny island, for twenty-seven years.

Sections were studied by means of the following special stains, in addition to the routine hematoxylin and eosin: congo red, sudan III, aniline blue (fig. 4), Verhoeff's elastic tissue stain (fig. 5), a modification of Cajal's trichrome stain, Van Gieson's stain and thionine (fig. 6).

The thionine stain proved to be of particular interest. Thionine is a strongly basic but metachromatic dye, useful chiefly because it stains mucin deep blue. It stains normal collagen and elastin only faintly. In these sections it was found to stain the colloid masses with

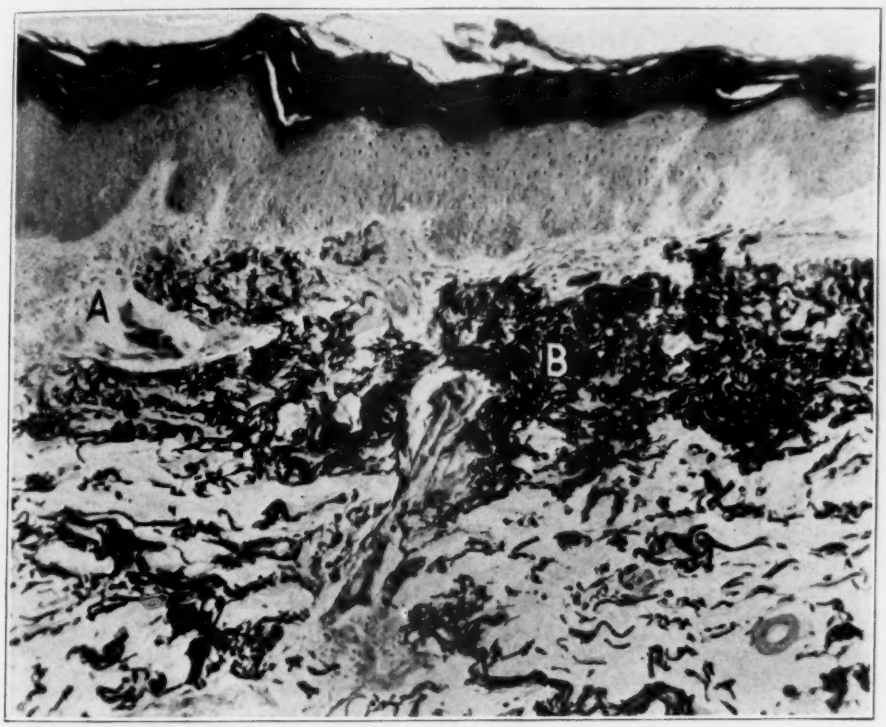

Fig. 5.—An incipient colloid "block" is shown at *A*, masses of deeply stained degenerated collagen and collacin, chiefly the latter, at *B*, and short, thick bundles of deeply stained elacin and perhaps a few fibers of elastin beneath. Collagen is unstained. Note that this is almost a photographic negative for figure 4. Verhoeff's elastic tissue stain (× 130).

remarkable intensity; unlike mucin, however, these did not give the acetic acid reaction. The basophilic collagen was also, as might have been expected with a basic dye, stained light blue. The more complexly degenerated connective tissue, however—the elacin and collacin—was stained deep blue, almost as dark a color as that of the colloid itself. Normal elastin, identified only in the deeper portions of the corium by Verhoeff's stain, was not stained by the thionine.

The results of the various connective tissue staining methods are summarized in the accompanying table. Stains for amyloid (congo red) showed that the colloid blocks had less tendency to take up the stain than the normal collagen did. Sudan III was taken up by the colloid to a moderate degree, but not nearly enough to suggest the presence of any significant amount of lipid material.

Fig. 6.—At *A* are seen a few fragments of colloid surrounded by a feltwork of degenerated collagen and collacin; at *B*, unstained collagen bundles intermingled with thick fibers of elacin; at *C*, only occasional fibers of elacin. Elastin and collagen are not stained by this method. Thionine (× 130).

Comparative Table of Special Connective Tissue Stains Employed

Tissue Structure	Hematoxylin and Eosin	Van Gieson's Mixture	Cajal's Trichrome *	Mallory's Aniline blue †	Verhoeff's Elastic Tissue Stain ‡	Thionine
Keratin.....	Bluish-red	Red-yellow	Green	Orange	Black	Light blue
Prickle cells.....	Blue	Tan	Gray-green	Pale gray	Unstained	Violet
Papillary collagen	Pink	Red	Blue	Blue	Unstained	Faint blue
Subpapillary collagen	Bluish	Brownish	Green	Light blue	Pale blue	Blue
Deeper collagen....	Red	Red	Blue	Deep blue	Unstained	Very faint blue
Elastin.....	Pink	Red	Blue	Blue	Blue black	Faint blue
Elacin.....	Pink	Faint pink	Blue	Faint blue	Blue-black	Deep blue
Collacin.....	Pink	Faint red	Blue	Unstained, or orange	Blue	Intense blue
Colloid.....	Bluish, with pink edges	Brown, with red edges	Green, with blue edges	Very pale blue with some orange areas and darker blue edges	Pale grayish blue, mottled	Purple, with pale edges

* Cajal's trichrome stain consists essentially of indigocarmine and picric acid (trinitrophenol) (Krajian, A. A.: Histological Technic, St. Louis, C. V. Mosby Company, 1940, pp. 106-107).

† An acid dye used in combination with orange G (Mallory, F. B.: Pathological Technique, Philadelphia, W. B. Saunders Company, 1938, pp. 153-154).

‡ This excellent stain is a mixture of hematoxylin, ferric chloride and iodine which must be freshly prepared each time it is used (Mallory, pp. 170-171).

COMMENT

It may be seen by reference to the table that the centers of the colloid blocks stained approximately the same color as the "degenerated" (basophilic) collagen, and the occasionally fibrillar-looking edges of the blocks stained approximately the same color as the normal collagen and elastin, with all of the strains.

Collacin (degenerated collagen plus elacin) was distinguished by its failure to take either aniline blue or orange G and by its intensely blue color with thionine. The clearcut, thick, short, slightly curved fibrils near the collacin masses, which stained so deeply both with thionine and with Verhoeff's stain, were assumed to be elacin (degenerated elastin). Elastin, stained by Verhoeff's method but not by thionine, was present only in very small amounts in the upper part of the corium and in larger quantity in the hypoderm. It does not seem that all this leads to any definite conclusions regarding the origin of the colloid; however, the extensive degeneration of both collagen and elastin suggests that both elements contribute to the formation of the colloid substance.

The failure of the colloid material to take up appreciable amounts of either congo red or sudan III was felt to exclude adequately any serious suspicion of either amyloid or lipoid degeneration. Control material run in parallel with the sections was stained well by both methods.

SUMMARY

Two types of colloid degeneration of the skin have been reported in the literature: a type with tiny multiple superficial papular lesions on the face, face and hands or hands alone, and a diffuse, deep variety; the latter is much the rarer.

Considerable confusion has been brought about by the use of a single term to designate both these entities, despite the fact that they have little in common either clinically or histologically.

The term "colloid pseudomilium" has been used on a number of occasions, particularly in Germany, France and South America, to designate the variety of colloid degeneration characterized by small papules.

A typical case of colloid pseudomilium, with study by means of several connective tissue stains, is presented herewith.

One of the stains employed, thionine, appeared to have the useful property of staining normal elastin and collagen not at all, degenerated collagen (basophilic collagen) only slightly, and elacin, collacin and colloid extremely deeply.

CONCLUSIONS

The variety of colloid degeneration of the skin originally described by Wagner and exemplified in the foregoing case should be regularly designated "colloid pseudomilium."

More extensive use of thionine in the study of senile and other degenerative processes in cutaneous connective tissue is suggested.

Dr. Irvin L. Tilden, of the Department of Clinical Pathology at The Clinic, prepared the sections, made the special stains and the photomicrographs and collaborated in the interpretation of the histologic changes.

881 Young Street at Thomas Square.

KERATODERMA CLIMACTERICUM (HAXTHAUSEN)

HYPOESTROGENIC KERATODERMATITIS

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ST. PAUL

Although not the first to describe a peculiar keratotic thickening of the palms and soles associated with the climacteric, Haxthausen [1] in 1934 presented a clear description of the eruption and noted its association with other evidences of the climacteric. He applied the term keratoderma climactericum to a "distinct clinical picture consisting of circumscribed hyperkeratosis, mainly of the palms and soles, occurring in women in association with the climacteric and accompanied by various general signs and symptoms, of which *obesity* and *arterial hypertension* are those most frequently encountered." This disease had received little attention before Haxthausen's report and even now is not often considered. There have been a few reports of cases, but both the dermatologic textbooks and those on endocrine diseases have given it little attention. Dermatologists should be more familiar with this keratosis, first, because it is more common than is generally realized; second, because its presence indicates a general endocrinologic disturbance, and, third, because it is one of the few dermatoses responsive to specific therapeutic agents.

In 1891, under the title "Notes on Some Keratoses of the Palms and Soles," Brooke [2] described a sharply circumscribed, chronic, dry, hard, thickened overgrowth of horny tissue on the palms and soles of a woman 47 years of age. Part of the eruption consisted of erythematous plaques, while the thicker lesions were "orange-grey." There was dull pain as well as tenderness, and movement was restricted because of the swelling and thickening. After persisting for eighteen months the eruption improved. The patient "complained of feeling nervous, and insisted that when excited or worried the redness and discomfort increased perceptibly. Quite possibly this irritability may have some connection with the approaching climacteric." Later in the same year Brooke [3] reviewed this case and reported on a similar eruption in a second patient, under the title "Erythema Keratodes of the Palms and Soles." The following year under the same title Dubreuilh [4] described another such patient and emphasized the erythematous raised border of the plaques. He regarded his case and Brooke's as "clear instances of a well defined disease," an opinion apparently held subsequently by authors of textbooks, who have continued to use a separate classification even since Haxthausen's report of 10 similar cases. I believe both groups of cases represent the same dermatosis.

There is confusion regarding keratotic eruptions on the palms and soles, as evidenced by the classifications in various "handbooks" and textbooks, probably

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From the Division of Dermatology (Dr. H. E. Michelson, Director) and the Students' Health Service (Dr. Ruth Boynton, Director).

1. Haxthausen, H.: Keratoderma Climactericum, Brit. J. Dermat. **46**:161, 1934.
2. Brooke, H. G.: Notes on Some Keratoses of the Palms and Soles, Brit. J. Dermat. **3**:19, 1891.
3. Brooke, H. G.: Erythema Keratodes of Palms and Soles, Brit. J. Dermat. **3**:335, 1891.
4. Dubreuilh, W.: Erythema Keratodes of the Palms and Soles, Brit. J. Dermat. **4**:185, 1892.

because diseases cannot easily be classified on a topographic basis, even though the differential diagnostic approach may have to start from that point. Moncorps [5] placed palmar and plantar eruptions in three main groups based on morphologic appearance: (1) diffuse, (2) plaquelike or striated and (3) punctate keratoses. Each group is subdivided according to its assumed origin: (*a*) idiopathic; (*b*) symptomatic. It is easy to see why dermatologists using this and similar classifications have failed to develop a satisfactory knowledge of a keratosis which is usually but not always symmetric, begins as a papule, enlarges to form a plaque and then a diffuse thickening and is a manifestation of a general condition whose nature might lead one person to classify the eruption as idiopathic while another would call it symptomatic. Undoubtedly this eruption has frequently been confused with the hereditary nevoid diffuse keratoses or mistakenly classified as psoriatic, but the majority of general physicians probably regard the patients as having mycotic dermatitis or eczema. In the scant literature and in the discussion of cases presented before societies it appears that dermatologists frequently regard the patients as having some form of hypothyroidism (even though the basal metabolic rate may be normal), or in more recent years a few observers have regarded the eruption as a dry, squamous or hyperkeratotic form of neurodermatitis.[6] Becker and Obermayer [7] give this subject more attention than most authors, and they discuss it as a special form of neurodermatitis which differs from the ordinary form "by the presence of rather extensive hyperkeratotic lesions on the ends of the toes."

The association of this eruption with the climacteric has given it particular interest. A number of other dermatoses are frequently associated with the climacteric, but only kraurosis vulvae appears to be at all comparable. The physiologic ovarian insufficiency of the climacteric ordinarily leads to atrophy of the external genitalia, yet in some cases dermatitis, abnormal thickening and hyperkeratosis are observed. The manner in which patients respond to estrogenic therapy is not uniform, and the pathogenesis of kraurosis is not entirely clear. As with keratotic thickening of the palms and soles, itching is a striking symptom.

CLINICAL FEATURES

According to Haxthausen, the eruption begins as a smooth, hyperkeratotic discrete round or oval papule, only slightly if at all elevated above the surrounding skin. In later stages he observed confluence of the lesions, eczematization with moisture and a tendency to development of fissures and loss of the sharp definition of the border of the lesions. Moderate itching was said to have been present after the eruption had become complicated with eczema. Some observers have emphasized the erythematous border which remains elevated after the central portion of the lesion becomes yellow, scaly and slightly depressed; others have pointed out the tendency to form fissures, which may be deep enough to result in bleeding, and some have observed itching or burning early in the course of the eruption.

The following description is based on observation of 10 cases of this disease. It usually begins with the development of one or several slightly elevated dull red

5. Moncorps, C., in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 8, pt. 2, p. 300.

6. (*a*) Brunsting, L. A., in discussion on Becker, S. W., and Obermayer, M. E.: Keratoderma Climactericum, Arch. Dermat. & Syph. **36**:646 (Sept.) 1937. (*b*) Engman, M. F., Jr., in discussion on Becker and Obermayer. (*c*) Weiss, R. S., in discussion on Becker and Obermayer.

7. Becker, S. W., and Obermayer, M. E.: Modern Dermatology and Syphilology, Philadelphia, J. B. Lippincott Company, 1940, p. 182.

to red-brown sharply circumscribed round or oval papules. Scaling is not prominent at first but becomes so as the papules enlarge and coalesce. The ultimate extent of the eruption varies within wide limits. It may remain as a single round or oval plaque with little scaling, situated at the border of the palm or sole or at the anteromedial border of the heel. More often the papules become plaques which coalesce and result in diffuse involvement of the central portion of the palms or the greater part of the soles, sparing the instep, which usually remains relatively free, though discrete lesions may occur there. The larger plaques are dry, thick and yellow-brown. The normal folds of the skin may become exaggerated to bleeding fissures, but usually there are only deep crypts between the thickened or

Fig. 1.—Characteristic extensive hypoestrogenic keratodermatitis with keratosis of the toes, relative freedom from involvement of the instep, heavy plaques at points of greatest pressure, crypts and fissures.

verrucous plaques of adherent scale (fig. 1). Thickening is especially prominent at the pressure-bearing points of the sole and heel, and crypts commonly appear proximal to the first metatarsophalangeal joint or just anterior to the heel, sites where the excessively thickened skin adjoins the softer skin of the instep.

The eruption often extends beyond the sole, and especially at the sides of the heels and on the medial plantar aspect there may be discrete papules or plaques. The nature of involvement of the toes is an important part of the clinical picture. Thickening of the skin is accompanied by yellow, adherent scaling, which is particularly evident on the anterior portion of the plantar surface of the toe near the free border of the nail.

As with other keratotic eruptions, the characteristic appearance may be modified or masked by the coexistence of mycotic infection. Suitable therapy improves the appearance of such eruptions but fails to relieve the symptoms.

In the series of cases reported by Haxthausen [1] the palms were involved in 5 instances, and in 6 both palmar and plantar involvement were recorded. It is my impression that the soles are more commonly involved but that patients are less likely to present themselves for treatment of plantar eruptions unless discomfort is more severe. Of the 10 patients included in this report, 9 presented plantar eruptions; in 5 the palms were also involved. In the remaining patient an eruption had been present for one year on one palm without extension to the other extremities. The interval between the appearance of plantar and palmar involvement varied from six months to five years. In 1 instance the patient regarded the eruption as of equal duration on all the extremities. In several instances where the palms were not involved, the feet had given trouble for two to four years. I find it difficult to venture any opinion as to why one or another area may be first involved or why certain areas may be spared. A relation with repeated trauma might be suspected, but in no instance in which both hands were involved did the patient note any difference in the time of onset on the two hands. In 1 case only the left palm was involved, and in 3 cases the left sole was involved first or exclusively. Such a distribution may result from an association with itching and right-handed scratching.

There is variance of opinion as to the presence of symptoms. Haxthausen stated that itching was absent in early stages and present to only a moderate degree after the appearance of eczematization. Goldberg [8] stated that "this form of keratoderma is not associated with any erythema or with subjective sensations of burning and itching," though the patient whose case he reported noted pain on walking. In contrast, itching and burning have been recorded by certain other authors and in most of my patients were the cause of considerable distress. Itching appeared as an early symptom and was severe in several patients. These particularly found that it was increasingly intense at night. Often these patients were unable to obtain relief by scratching and complained that the itching was deep in the skin. Itching was often accompanied or followed by intense sensations of burning heat (not associated with "hot flashes"). Scratching, pinching and rubbing were frequently resorted to, and these manipulations may be the chief cause of the eczematization which occurs in severe eruptions. Bleeding from the fissures was observed only when eczematization was present. Eczematization was not accompanied with the appearance of macroscopic vesicles.

The ages of the patients varied within wide limits, 29 to 62 years, but 7 were 52 to 62 years of age and had reached the period during which women usually enter the third and final stage of the climacteric (permanent estrogenic deficiency).

Haxthausen enumerated obesity, hypertension and rheumatoid pains as commonly associated with this disease. No accurate record was kept of weights of the patients in the present series, but most of them were moderately overweight and several were obese. The 29 year old woman was only slightly above the average weight for her age and height. Her blood pressure was 120 systolic and 76 diastolic, while that of 5 other patients was 180 and 90, 170 and 100, 160 and 90, 155 and 80 and 130 and 80 respectively. Pain or swelling of one or more joints was noted in 4 of 7 patients concerning whom inquiry was made.

8. Goldberg, L. C.: Keratoderma Climactericum, Arch. Dermat. & Syph. **40**:67 (July) 1939.

COURSE AND TREATMENT

The course of the eruption varies within wide limits. Particularly in milder forms of the disease the severity of the eruption may be variable; it may even disappear and then recur later. In view of its association with the climacteric, one would expect the eruption to disappear spontaneously after months or years; yet in 1 patient it persisted for twelve years before specific treatment was given.

The degree and duration of itching and burning are variable. This was emphasized in the initial reports by Brooke and is well demonstrated in several cases in this series. The symptoms may increase and decrease in relationship with the more general symptoms of the climacteric.

Haxthausen was discouraged with the results of treatment for his patients, but subsequent attempts resulted in greater success. Goldberg's [8] report was of particular interest because of the response of his patient to biweekly injections of estrone and therapy with unfiltered roentgen rays at weekly intervals, with complete cure after two months. When estrone was administered orally Bishop and Barber [9] noted improvement in three weeks. Wolf's [10] patient failed to obtain relief after six weeks of similar treatment.

All patients in this series have been given diethylstilbestrol, and in the 7 for whom adequate dosage was possible there was benefit from its administration. I have usually begun treatment with 0.1 to 0.25 mg. of diethylstilbestrol daily and increased the dosage according to tolerance. Of the 3 patients for whom benefit was not recorded, 1 failed to continue treatment and 2 did not return for further observation. One must not become discouraged with the early results of treatment. It seems that an initial satisfactory response is likely to be followed by a period when fissures and desquamation persist; only later does the palm or sole become soft and pliable (fig. 2). The refractory period seems to be due to the time necessary for casting off the thick keratotic plaques which have been firmly adherent. As some of the hyperkeratotic material separates, cracking may develop at the border of the area where separation occurs. Though most of the itching and burning are likely to be relieved after two to three weeks of treatment several months are required for complete relief of symptoms and for disappearance of the eruption.

HISTOPATHOLOGY

Discussion of the pathologic process has usually been based on Haxthausen's report of sections from a single patient in which he noted increased thickening of the horny layer, with fraying of the individual cell layers. Circumscribed areas of parakeratosis were described. There were no microabscesses, miliary vesicles or vacuolar formations in deeper lying cells of the epidermis. Acanthosis was not observed. The corium was said to have been normal except for round cell infiltration along the vessels.

The following description is based on a study of 5 specimens removed from the feet of 3 patients and from the palm of 1 patient on whom biopsy was also performed a second time after a five year interval. The two sections from the latter patient were similar in spite of the prolonged period between the times of removal. They presented extensive hyperkeratotic thickening of the stratum corneum without evidence of parakeratosis. The papillae showed greatly increased vascular supply

9. Bishop, P. M. F., and Barber, H. W.: Keratoderma Climactericum (Haxthausen) Treated with Oestrone, Proc. Roy. Soc. Med. **30**:738, 1937.

10. Wolf, J.: Keratoderma Climactericum, Arch. Dermat. & Syph. **43**:731 (April) 1941.

with numerous dilated capillaries (fig. 3). Both in the papillary region and throughout the upper cutis the larger vessels had thickened walls and swollen endothelium.

The sections from the feet showed considerably greater inflammatory reaction. Hyperkeratosis was present to a pronounced degree in all specimens, and small areas of parakeratosis were present in 2. The rete pegs were elongated but not broadened. A few small lymphocytes were seen between the epithelial cells. At

Fig. 2.—Mottled appearance of the heel after separation of heavy scale and thickened skin in a case in which eczematization had previously been present.

the tips of some papillae there were localized changes which cannot be spoken of as "microabscesses" but which consisted of small areas of degeneration of epithelial and connective tissues, a moderate number of small lymphocytes (no polymorphonuclear leukocytes) and intercellular edema in the adjacent epidermis (fig. 4). Scattered in the papillary layer of the cutis and the midcutis were other small areas of infiltration with numerous small and some large lymphocytes. In the deeper portion of the cutis the infiltrate was limited to the perivascular region. The blood

vessels of the upper part of the cutis and the midcutis showed endothelial swelling and thickening of their walls. Special stains demonstrated swelling of the collagenous fibers and fragmentation and degeneration of many of the small and large fibers of elastin.

From this description it must be obvious that one can exclude most of the keratotic eruptions which might be confused clinically. According to Gans [11] the hereditary nevoid form of symmetric keratosis presents thickening of all the epithelial strata, including the stratum lucidum, but there are no inflammatory

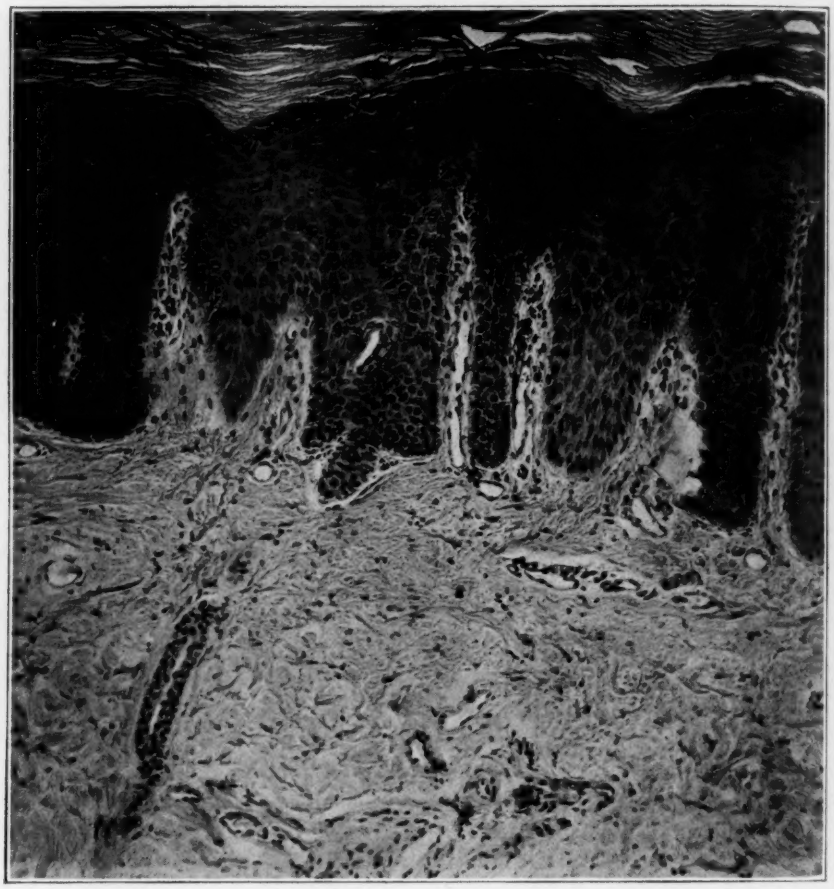

Fig. 3.—Lymphocytic infiltration and vascular changes in a section from the palm.

changes and the cutis is normal. There is greater difficulty in differentiating this disease from neurodermatitis. Dermatologists frequently disagree in the clinical diagnosis of neurodermatitis, and histologic studies of sections from the palms and soles have not been described in sufficient detail so that the disease can be recognized microscopically. Vascular thickening, endothelial swelling and edematous and degenerative changes in the connective tissue fibers may be more characteristic of the keratodermatitis associated with ovarian insufficiency, but in the patients whom I examined the histologic changes must be pronounced as not pathognomonic for either condition. Microscopically it is difficult or impossible to differentiate

11. Gans, O.: Histologie der Hautkrankheiten, Berlin, Julius Springer, 1925, vol. 1, p. 55.

this disease from neurodermatitis. The existing reports of microscopic studies are too few to allow one to depend on relatively minor differences.

CHOICE OF TITLE

The National Conference on Nomenclature of Disease did not include the term "keratoderma climactericum" in its recent revision of the Standard Nomenclature of Disease.[12] For all of the diseases formerly entitled keratoderma the committee responsible for the dermatologic nomenclature prefers the use of the term keratosis.

Fig. 4.—A section from the side of the heel showing hyperkeratosis, slight parakeratosis, elongation of the rete pegs, lymphocytes in the epithelium and the cutis, focal areas of intercellular edema and degenerative changes.

However, this eruption gives clinical and microscopic evidence of inflammation in many cases, and for this reason Becker [13] has suggested that it should be referred to as a dermatitis. The term "keratodermatitis" may be the most satisfactory, because scaling and thickening are prominent features of the disease.

There is a further reason why Haxthausen's term is not completely acceptable; this eruption need not be associated with the climacteric. The age of 1 of Brooke's

12. Fox, H.: Standard Nomenclature of Disease, Arch. Dermat. & Syph. **46**:534 (Oct.) 1942.

13. Becker, S. W.: Personal communication to the author.

patients and 1 of mine was less than 30 years, and there was no evidence that the climacteric was approaching. A suitable title should be capable of application to all patients having keratosis of the palms and soles due to ovarian inactivity, regardless of age. Even if it may be assumed that the eruption results from ovarian insufficiency the term "hypo-ovarian" would not convey the proper meaning to many clinicians who apply it to the ovarian inactivity which results from congenital defects or from so-called primary ovarian failure; the term is less commonly used in reference to the physiologic ovarian failure of the climacteric. A deficiency of estrogen appears to be the most important factor in the development of the eruption, though other internal secretions may also be involved. Taking all these points into consideration, it would seem that the disease should be spoken of as "hypoestrogenic keratodermatitis of the palms and soles" (keratodermatitis hypoestrogenica palmaris et plantaris) rather than "keratoderma climactericum."

RELATION TO NEURODERMATITIS

The relation between neurodermatitis and hypoestrogenic keratodermatitis deserves considerable attention because it is a point about which there is much disagreement. Probably much of the difference in opinion results from lack of a common understanding of the term neurodermatitis, which must be defined by each author before the reader can know what is meant. Some dermatologists have no belief in the existence of neurodermatitis of the palms and soles; others use the terms moist or dry neurodermatitis to refer to the eruptions formerly described as tylotic eczema. While the latter term is useful because it is descriptive, the term neurodermatitis will be used because it points out the important relationship to nervous tension, though the nature of this relationship is none too clearly understood. I do not here use the term neurodermatitis as a synonym for "atopic eczema or dermatitis."

The dermatologic features of the disease known as keratoderma climactericum do not allow easy differentiation from neurodermatitis; thickened, scaling palmar eruptions may fall in either category. Plantar eruptions are common in keratodermatitis associated with the climacteric, while many dermatologists hesitate to make the diagnosis of neurodermatitis when the eruption is limited to the soles. The dry forms of neurodermatitis observed elsewhere on the body do not commonly produce the extreme degree of thickening and the verrucous changes so characteristic of plantar keratodermatitis, but this variation may be due only to the differences in location. Itching is the most striking feature of neurodermatitis, while the presence of burning is more complained about by patients having keratodermatitis. It must be agreed that the clinical features do not allow clear differentiation between hypoestrogenic keratodermatitis and neurodermatitis of the palms or soles and that microscopic differentiation is probably impossible.

In a recent consideration of neurodermatitis of the palms and soles Mary Smith [14] was hesitant or unwilling to regard as keratoderma climactericum any eruption with which there was evidence of neurodermatitis in other locations. In contrast, Haxthausen included in his series 2 patients presenting additional eruptions, 1 on the dorsa of the hands and the other on the knees, and I have included in my series 3 patients presenting an associated or complicating neurodermatitic eruption. One woman had scaling and thickening in each prepatellar area; another had an itching eruption at the nape of the neck; the third had suffered from itching papular axillary dermatitis. Many of the patients reported on by

14. Smith, M. S.: Lichen Simplex Chronicus (Neurodermatitis) of the Palms and Soles, Brit. J. Dermat. **54**:255, 1942.

Haxthausen made little or no complaint of itching, and Mary Smith expressed the opinion that the presence of itching rules against a diagnosis of keratoderma climactericum. She also suggested that abnormal sugar tolerance curves are likely to be demonstrable in patients with neurodermatitis. Haxthausen noted the presence of vascular hypertension in patients with keratoderma climactericum, and Mary Smith regarded its presence as a point of differentiation from neurodermatitis; yet Becker [13] suggested that "functional hypertension is not uncommon in patients with neurodermatitis." All these statements suggest the difficulty encountered in trying to differentiate the two diseases.

One who would separate hypoestrogenic keratodermatitis and neurodermatitis must offer a satisfactory explanation of the presence of the latter disease in 2 patients in Haxthausen's series and in 3 of mine, in whom the clinical evidence on the palms and soles was characteristic. A possible explanation follows the knowledge that the neurodermatitic woman will inevitably enter her climacteric and that the woman of a personality susceptible to neurodermatitis will probably have that susceptibility increased at times of ovarian dysfunction. Thus, if the two eruptions represent distinct diseases it is possible that at least some women with hypoestrogenic keratodermatitis might also have neurodermatitis at some other site.

Evidence of ovarian insufficiency may be the most important point of distinction between the two groups of patients. Though ovarian insufficiency is evident in many women who present neurodermatitis, it is by no means constantly observed. Neurodermatitis usually appears early in life, often in the third decade, while hypoestrogenic keratodermatitis in most cases appears much later, in the terminal phase of the climacteric. Estrogenic therapy is helpful to many patients with neurodermatitis, but in hypoestrogenic keratodermatitis the use of estrogenic agents appears to be of much greater and more constant benefit; it is perhaps essential in effecting a permanent cure. Nervous tension is evident in patients with both diseases, but emotional instability is more constantly observed in the presence of ovarian insufficiency. Vascular hypertension, obesity and rheumatoid pains are common accompaniments of hypoestrogenic keratodermatitis but are not particularly noted in neurodermatitic patients outside of the climacteric period. The presence of menstrual abnormality, general depression or a feeling of exhaustion, occipital headache or nuchal tension suggests that a patient has ovarian insufficiency rather than ordinary nervous tension.

Shortly after Haxthausen described this disease Barber [15] stated his belief that the patients belonged in the same group with some he had studied. In his series of 6 patients there were as many men as women, and the uric acid level in the blood was high "in nearly all." The 3 women were aged 26, 39 and 70 years, and only the last had vascular hypertension. Barber apparently thought it impossible to distinguish clinically between the eruptions described by Haxthausen and those which he had observed in males. In a later report he expressed a belief that such examples fall into two groups, one in which the eruptions are associated with the menopause, and a second in which men predominate and gout is associated. In spite of Barber's observations, there has been a relative paucity of reports of this type of eruption in men, a lack which might be cited as suggestive evidence of the hypoestrogenic nature of the disease were it not for the fact that neurodermatitis of all types is so much more common among women.

15. Barber, H. W.: Symmetrical Hyperkeratosis of the Palms and Soles, Brit. J. Dermat. **46**:95, 1934.

The uric acid level was normal in the cases reported as keratoderma climactericum by Goldberg [8] and Becker and Obermayer.[7] In 3 cases in the present series the levels were 1.8, 2.2 and 5.0 mg. per hundred cubic centimeters of blood.

RELATION TO THYROID DISEASE

It has long been known that scaling palmar eruptions may be associated with endocrine disorders. In some instances the hereditary nevoid form of symmetric keratosis has been associated with hypogenitalism, infantilism or incomplete development of the internal genital structures.[16] Such cases may represent an association of developmental defects rather than a causal relationship. Patients with pituitary disease frequently have thickened, dry palms. In old age one sees dry scaling eruptions, though thickening is not particularly evident; the use of testosterone has occasionally been credited with relief of such changes.[17] A relationship between palmar eruptions and diabetes has been noted by a few dermatologists.[18] Hypothyroidism, too, results in palmar changes, which may respond to administration of thyroid substance.[19] This relationship is so well known that it has been suggested [20] that the eruption in Haxthausen's patients may have been due to hypothyroidism in spite of the failure of thyroid treatment.

The basal metabolic rate was determined for only 2 of my patients. The rate of the one was + 5 per cent, and that of the other varied from + 7 per cent to + 29 per cent in four tests over a period of four years. Thyroid was not administered to any of my patients, because most previous reports on its use have been unfavorable or without enthusiasm.

DIFFERENTIAL DIAGNOSIS

Recognition of this type of keratodermatitis of the palms and soles is chiefly dependent on familiarity with the disease. In most cases one can readily exclude the possibilities of mycotic dermatitis, syphilis, psoriasis and keratosis blennorrhagica. Mycotic infection usually involves the interdigital webs and the toes. Though these tissues may be affected when fungous infection complicates hypoestrogenic keratodermatitis, the instep is not likely to show severe involvement unless fungous infection is primary. Psoriasis usually provides other evidence of its presence. Papular syphilids can easily be excluded from the diagnostic possibilities, and the serologic reaction or additional clinical evidence will relieve any doubt in cases in which plaques are present and clinical differentiation might present any difficulty. Keratosis blennorrhagica may be preceded by vesicles or vesicopustules. In later stages removal of the crust exposes a moist, inflamed

16. (*a*) Mierzecki: Keratoderma palmare et plantare hereditarium, Zentralbl. f. Haut- u. Geschlechtskr. **21**:141, 1926. (*b*) Sutejec, G.: Klinik und Pathogenese der familiären symmetrischen Keratodermie, ibid. **24**:798, 1927. (*c*) Olmsted, H. C.: Keratodermia Plantaris et Palmaris Congenitalis, Am. J. Dis. Child. **33**:757 (May) 1927.

17. Henschen, C.: Ueber das Keratoderma senile volae manuum et plantae pedum und seine Heilung durch Perandren, Schweiz. med. Wchnschr. **70**:690, 1940.

18. (*a*) Bechet, P.: Keratosis Plantaris, Arch. Dermat. & Syph. **46**:762 (Nov.) 1942. (*b*) MacKee, G. M., in discussion on Bechet.

19. (*a*) Mussio-Fournier, J. C.: Kératodermie plantaire et palmaire chez une hypothyroïdienne, Bull. et mém. Soc. méd. d. hôp. de Paris **48**:1236, 1932. (*b*) Niles, H. D.: A Case for Diagnosis (Keratoderma Palmare Symmetricum), Arch. Dermat. & Syph. **34**:1051 (Dec.) 1936. (*c*) Guy, W. H., and Jacob, F. M.: Keratoderma Plantare, Arch. Dermat. & Syph. **36**:1285 (Dec.) 1937. (*d*) Cervino, J. M.; Bertolini, A., and Larrosa Helguera, R. A.: Keratodermias of the Hands and Feet and Thyroid Deficiency, Endocrinology **22**:615, 1938.

20. (*a*) Engman.[6b] (*b*) Weiss.[6c]

surface, whereas the thickened scale of hypoestrogenic keratodermatitis cannot easily be removed.

Diagnostic consideration of neurodermatitis of the palms and soles always leads to confusion because of the failure of dermatologists to agree as to the existence and the nature of the disease. If there is a moist form of neurodermatitis (as I believe there is), the presence of macroscopic vesiculation distinguishes it from hypoestrogenic keratodermatitis. The dry, chronic form of neurodermatitis affords greater difficulty, and the question as to the possibility of its differentiation is discussed in detail in a preceding section of this paper.

SUMMARY AND CONCLUSIONS

Attention is called to the fact that Brooke appears to have been first to report a peculiar keratotic thickening of the palms and soles which was later described by Haxthausen as keratoderma climactericum. In this paper 10 cases of that disease have been reviewed in an attempt to clarify certain of the confusing features. While agreeing with the main points of Haxthausen's description of this dermatosis, I believe that plantar involvement is more common than palmar and that itching and burning are likely to be present long before eczematization is evident.

A description of the histologic changes produced by this disease is based on study of 5 specimens, several of which presented a greater degree of inflammatory reaction than was noted in the case studied by Haxthausen. Swelling of the collagenous fibers and degeneration of the elastin were also noted.

In most cases a favorable effect followed the administration of diethylstilbestrol for as short a period as one or two weeks. For cure or greater degrees of relief the treatment had to be continued for several months. The results could probably have been improved by attention to the more strictly dermatologic approach, but dependence on endocrine therapy afforded stronger evidence of the nature of the disease.

The relation with neurodermatitis is discussed in considerable detail. It does not seem possible to point out clinical or microscopic features which allow differentiation of hypoestrogenic keratodermatitis from neurodermatitis. A few dermatologists deny the existence of neurodermatitis of the palms and soles; many believe that neurodermatitis is always dry and never moist, and still others apply the terms moist and dry neurodermatitis to those eruptions formerly referred to as dyshidrotic or tylotic eczema. If they are separate disorders they have many features in common and must be closely related. It is my belief that the palmar and plantar eruption described by Brooke and generally known as keratoderma climactericum (Haxthausen) is a form or variant of neurodermatitis; yet there are features which suggest that it should be considered in a somewhat different category. The eruption is associated with evidence of disturbed estrogenic activity in so large a proportion of cases that one is forced to regard the association as of major etiologic significance. The favorable clinical response to administration of estrogens is more striking than the occasional moderately favorable influence of these agents on the more common forms of neurodermatitis. These reasons lead me to believe that the disease will be recognized more generally and treated more intelligently if such cases are described under another title rather than the broad and frequently misunderstood term "neurodermatitis." Because the disease occurs also in women who have evidence of endocrine disorder but are not approaching or passing through the climacteric and because the term keratoderma is not acceptable to authorities on nomenclature, I suggest that "hypoestrogenic keratodermatitis of the palms and soles" is a more suitable title for this disease than the terms applied by Brooke or by Haxthausen.

THE MOSAIC FUNGUS

A CHOLESTEROL INTERCELLULAR ARTEFACT

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HENRY C. SCHORR, M.D.

AND

HANS POPPER, M.D.

CHICAGO

All who have used direct methods in examining scales from the palms and soles for the presence of fungi have not infrequently been disconcerted by finding the mosaic fungus. It is a form that assumes geometric figures that trace the outlines of the cells in the scale. The mosaic material does not cross the body of the cells but always remains at their periphery.

Weidman,[1] who gave this form its name, had this to say about it:

> . . . the segments are irregularly shaped, and are separated from each other by narrower or broader, but definite, spaces; they have a moth-eaten appearance, and their edges and corners are rounded off. They do not have any organized internal structure; arthrospores are not visible within the segments. But it is the *arrangement* of the mycelium that raises the question whether this is fungus—not so much that it occurs in smaller and larger patches, but that the mycelium ramifies and anastomoses around the individual epidermal cells in such a way as to suggest that air or other refractile matter had become imprisoned between the cells. These hyphae vary in width, until finally one recognizes only thread-like filaments coursing between the cells. It requires fine discrimination to come to the conclusion that these are fungous and not inert intercellular accumulations. I have applied the term "mosaic" to this form because, following as they do the intercellular clefts, the hyphae come to surround smaller and larger polyhedral spaces, which collectively give the "pavement" effect.

He regarded as fungous only those growths in which the "mosaic" is abundant and definitely branching, the hyphae being continuous and the sides parallel.

Bruhns and Alexander[2] considered the mosaic form to be an artefact and referred to it as "pseudofungus." They stated that it was due to potassium hydroxide solution which had become diffused in the intercellular spaces. They expressed the opinion that in some cases the picture could be produced by air occupying these spaces.

Greenwood and Rockwood[3] were able to demonstrate the presence of the mosaic forms together with normal mycelium in the same scale. MacKee and Lewis[4] too found specimens in which the mosaic fungus mingled with the fungi which cause ordinary dermatomycosis. The latter authors could find the mosaic fungus in the roofs of artificially raised blisters on apparently normal skin. They expressed the opinion that the weight of evidence was in favor of its being a

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1. Weidman, D.: Laboratory Aspects of Epidermophytosis, Arch. Dermat. & Syph. **15**:415 (April) 1927.

2. Bruhns, C., and Alexander, A., in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol. 11, pp. 89 and 464.

3. Greenwood, A. M., and Rockwood, E. M.: The Skin in Diabetic Patients, Arch. Dermat. & Syph. **21**:96 (Jan.) 1930.

4. MacKee, G. M., and Lewis, G. M.: Keratolysis Exfoliativa and the Mosaic Fungus, Arch. Dermat. & Syph. **23**:445 (March) 1931.

degenerated fungus. They held that the lesions where it was found were caused by a dissemination of fungi from an original focus but that the organisms become altered because the environment had become unfavorable—in short, that the mosaic fungus represents the result of an only partially successful immune process set up by the host.

Davidson and Gregory [5] came to the conclusion that the mosaic fungus consists principally, if not entirely, of crystals of cholesterol. They were able to

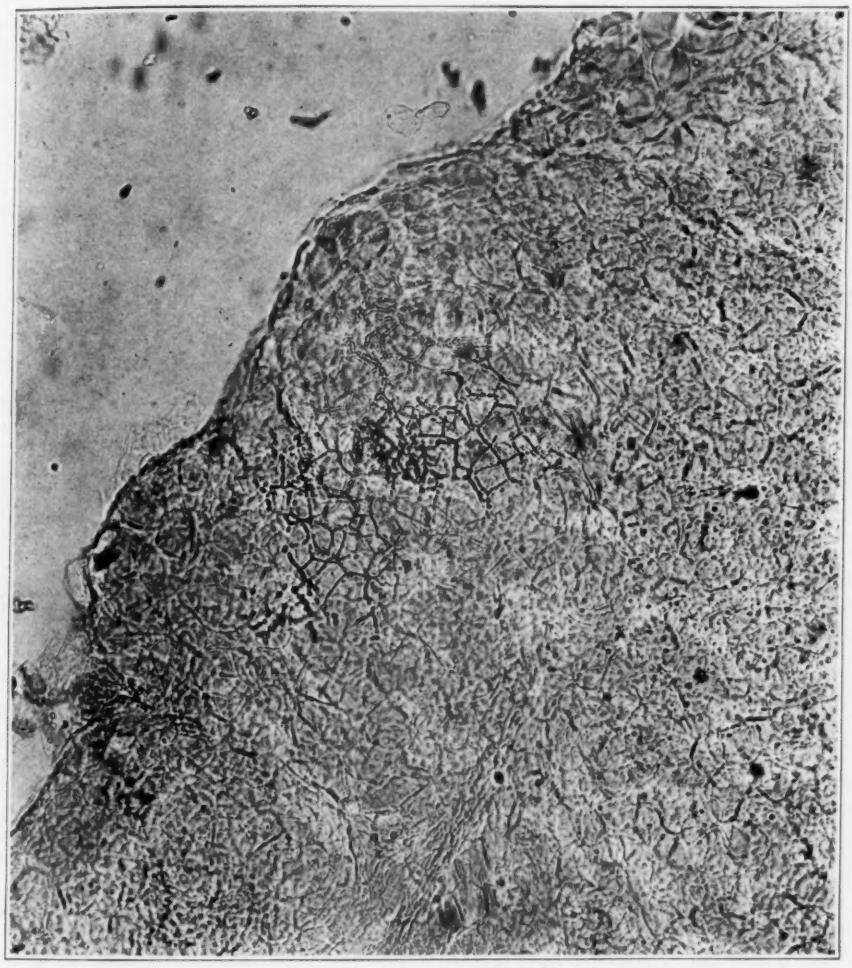

Fig. 1.—Alkali preparation of scales showing the mosaic fungus.

observe these crystals with a magnification of about 930 diameters. The illustrations accompanying their report give weighty evidence in support of their position. Downing,[6] in a discussion of this presentation, reported that with sulfuric acid and iodine he had obtained tinctorial evidence of the presence of cholesterol.

5. Davidson, A. M., and Gregory, P. H.: The So-Called Mosaic Fungus as an Intercellular Deposit of Cholesterol Crystals, J. A. M. A. **105**:1262 (Oct. 19) 1935.

6. Downing, J. G., in discussion on Davidson and Gregory.[5]

Dowding and Orr [7] expressed the opinion that the mosaic growth is of fungous origin. They found mosaic segments in tissue joined end to end with Trichophyton gypseum hyphae and also close to the ends of the hyphae but not in actual contact. They observed normal fungous spores and traces of hyphae to make up part of the mosaic formation. Furthermore, they found that during the healing of lesions of a patient suffering from Trichophyton gypseum infection the mosaic fungus increased and the living fungus decreased.

This conflicting evidence and opinion led us to undertake new studies for more evidence. Increasing use is being made in clinical dermatology of the fluorescent

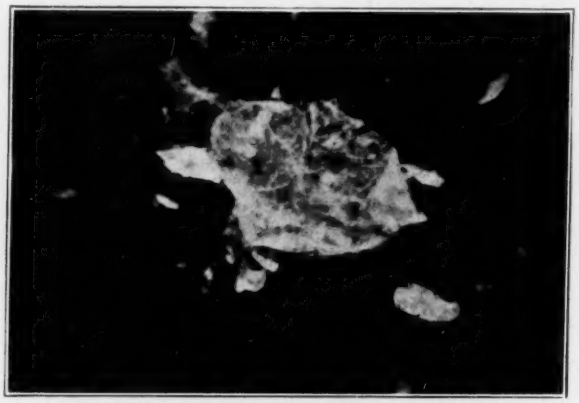

Fig. 2.—Scale from pityriasis versicolor as viewed through the fluorescence microscope.

Fig. 3.—Scale from scalp with fungi viewed through the fluorescence microscope.

properties of fungi. Clinics are finding indispensable the use of fluorescence modalities for the observation of fungous infections, for diagnosis and to control therapy. Cultures of fungi may be subjected to fluorescence to aid in their classification.

By means of fluorescence microscopy we have been able to demonstrate a characteristic ultraviolet stable green fluorescence in scales, hair and nails harboring various fungi. This green fluorescence differed from the blue and bluish gray fluorescence emitted by uninfected tissues themselves. In scales in which mosaic

7. Dowding, E. S., and Orr, H.: Transformation of Trichophyton Gypseum into Mosaic Fungus, Arch. Dermat. & Syph. **33**:865 (May) 1936.

structures were demonstrated only the dull bluish fluorescence of the scales but no bright green fluorescence of fungi was found. The area where in visible light the mosaic structure was seen did not impart a characteristic fluorescence.

Phosphin 3R is a water-soluble fluorescent stain for fat which produces a bright silver white fluorescence of fat against a dull brown fluorescent background.[8] On scales showing mosaic fungus it produced a silver white fluorescence of the mosaic structure, the scales themselves fluorescing dull brown. When the specimens

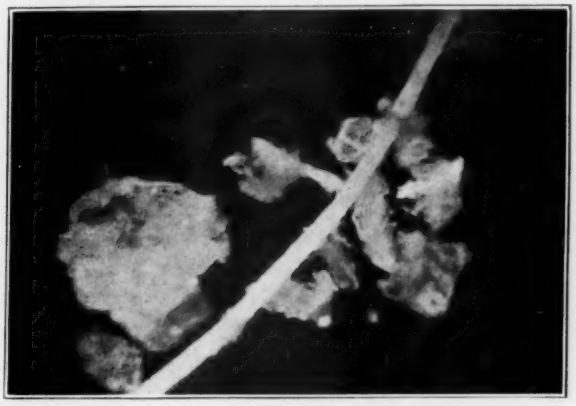

Fig. 4.—Hair and scales from scalp (same case as fig. 3).

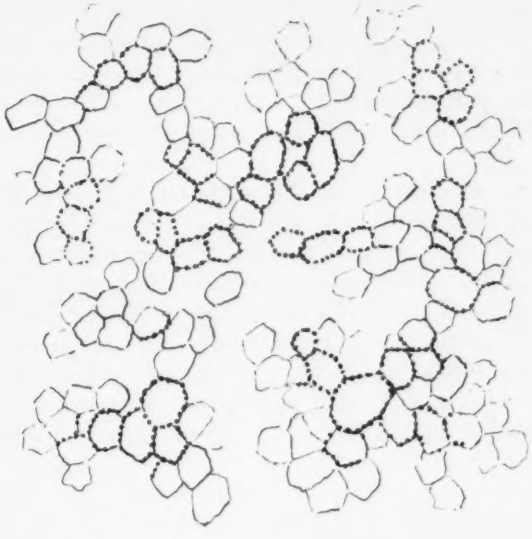

Fig. 5.—Drawing of preparation made from scale of keratolysis exfoliativa using the Liebermann-Burchard reaction.

were first treated with acetone for ten minutes, phosphin 3R failed to produce the silver white fluorescence of the mosaic structure, and only the dull brown fluorescence of the scales was noted. In polarized light the mosaic structure appeared as doubly refractile ramified branched needles. After the scales were soaked in acetone the double refraction was no longer evident.

8. Popper, H.: Histologic Distribution of Vitamin A in Human Organs Under Normal and Under Pathologic Conditions, Arch. Path. **31**:766 (June) 1941.

Schultz [9] has adopted the Liebermann-Burchard color test for cholesterol for use in tissue. It is said to be specific for cholesterol whether free or as an ester. The reaction is never positive if cholesterol is absent, but it sometimes may be negative when cholesterol is present. Using Schultz's technic we obtained a positive reaction for cholesterol at the site of the mosaic fungus.

COMMENT

It seems clear from the work of others and our own observations that cholesterol is present in the mosaic fungus. Is it alone responsible for the phenomenon of the mosaic fungus? Differential fat solvents show that the material demonstrated by the fluorescent fat stain phosphin 3R is not lecithin, since the silver white fluorescence is removed if the scales are first treated with acetone before staining. Acetone does not dissolve lecithin and hence would not remove it.

Is the cholesterol in the mosaic fungus a product of a previously living fungus? It has been found associated with living fungi in some instances, though not in actual contact. It is claimed that as the lesions in which it is found improve, the ordinary fungous elements decrease while the mosaic fungus increases. In none of such situations has the transition product been seen. It is probably reasonable to suppose that there would not be a sudden and abrupt transformation of living fungus to cholesterol. There should undoubtedly be intermediate steps in such a conversion, such as one sees between basal epidermal cells and keratin.

Ordinary fungi traverse cells and grow in straight lines. The mosaic fungus never does this but is always found outside the confines of the cells. It is difficult to visualize the process by which a living fungus would be pushed aside and out of the keratin cells. Where a living fungus and the mosaic fungus are associated, disintegration of the hyphae unquestionably should be seen, with tracks of cholesterol leading through the parasitized cell to its border. This has not been observed. Only independent autochthonous elements are seen without transitions traceable through cells.

The mosaic fungus is found almost exclusively in processes where vesicles are of the so-called dry type and poorly distended or where leaves of epidermis separate without accumulating material beneath them. Does the death of the previously living fungus before the appearance of cholesterol cut short the attraction of fluid elements? Cholesterol is a hydrophobe and in itself would not attract water.

It is known that phospholipids are relatively plentiful in the lower strata of the epidermis, whereas cholesterol is the predominating lipid in the keratin layer. The mosaic fungus is found, among other places, invariably in the lesions of keratolysis exfoliativa. Could this disease represent an anomaly of keratinization with excessive presence of cholesterol? Could the excessive presence of cholesterol in the horny layer cause it to separate? Perhaps this may give the clue to the means by which the normal exfoliation of epidermis takes place—the physiologic accumulation of cholesterol at the surface of the skin.

SUMMARY

The literature is cited to show that there is a difference of opinion regarding the mosaic fungus. One school of thought believes it is a real fungus or at least a degenerated living fungus, whereas a second considers it an artefact.

Experiments are reported in which by fluorescence microscopy and otherwise, the mosaic fungus was found not to display certain properties of living fungus.

9. Schultz, cited by Mallory, F. B.: Pathological Technique, Philadelphia, W. B. Saunders Company, 1938.

Evidence obtained by examination in polarized light and with fluorescent dyes and by solubility tests and specific staining methods was presented for the presence of cholesterol or cholesterol compounds at the sites occupied by mosaic fungus.

These results and the evidence of others are discussed to support the belief that the mosaic fungus is not a true fungus or developed from a true fungus.

The idea is developed that the mosaic fungus represents accumulations of cholesterol in an anomalous process of keratinization where an excess of the lipid is formed or is present.

The theory is suggested that cholesterol may be responsible pathologically for the separation of the leaflets of scale in keratolysis exfoliativa and physiologically for the normal exfoliation of the epidermis.

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PITYRIASIS RUBRA PILARIS OF FAMILIAL TYPE

EXPERIENCES IN THERAPY WITH CAROTENE AND VITAMIN A

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The superficial clinical resemblance of certain cutaneous diseases to the phrynoderma of clinical and experimental vitamin A deficiency has led to a reconsideration of such conditions as possible manifestations of avitaminosis A. Among them are keratosis pilaris [1] (ichthyosis follicularis, lichen pilaris, etc.), Darier's disease [2] (keratosis follicularis) and pityriasis rubra pilaris.[3]

Lehman and Rapaport [1] studied a group of 9 children who exhibited the lesions of keratosis pilaris. They observed that the photometric values for dark adaptation as determined by the biophotometer were abnormal for these patients and that both this defect and the cutaneous lesions were for the most part corrected by administration of vitamin A. They concluded that keratosis pilaris and its synonyms were manifestations of vitamin A deficiency. Peck, Chargin and Sobotka [2] successfully treated Darier's disease with vitamin A and interpreted this condition as a "physiologic nevus with a hereditary weakness in vitamin A absorption or in conversion of provitamin A to vitamin A." Pettler [3a] was apparently the first to suggest that pityriasis rubra pilaris might be a manifestation of vitamin A deficiency. He observed beneficial effects on the cutaneous lesions after administration of vitamins A, B and D to 3 patients with acquired pityriasis rubra pilaris. Laboratory studies were not performed. Recently Brunsting and Sheard [3c] studied dark adaptation in acquired pityriasis rubra pilaris by means of a new method. They found an elevated threshold in 3 patients, all of whom showed a striking improvement after treatment with vitamin A and other vitamins. The response of the cutaneous lesions, however, was less dramatic and less complete.

This report is concerned with the study from the standpoint of vitamin A deficiency of 5 patients with familial pityriasis rubra pilaris. More especially it concerns the effect of the administration of carotene and vitamin A on dark adaptation and on the cutaneous manifestations of the disease.[4]

MATERIAL AND METHODS

The family involved in this experimental study consisted of a mother and her 4 children all of whom had clinical (and histologic) pityriasis rubra pilaris. It

From the departments of dermatology and ophthalmology of the University of Cincinnati College of Medicine and the Cincinnati General Hospital.

1. Lehman, E., and Rapaport, H. G.: Cutaneous Manifestations of Vitamin A Deficiency in Children, J. A. M. A. **114**:386-393 (Feb. 3) 1940.

2. Peck, S. M.; Chargin, L., and Sobotka, H.: Keratosis Follicularis (Darier's Disease): Vitamin A Deficiency Disease, Arch. Dermat. & Syph. **43**:223-229 (Feb.) 1941.

3. (*a*) Pettler, M. F.: Pityriasis Rubra Pilaris with Particular Reference to Vitamin Medication and Dietary Control, Pennsylvania M. J. **39**:864-866 (Aug.) 1936; (*b*) Effect of Vitamin A in Pityriasis Rubra Pilaris and Keratoses Follicularis, ibid. **45**:604-605 (March) 1942. (*c*) Brunsting, L., and Sheard, C.: Dark Adaptation in Pityriasis Rubra Pilaris, Arch. Dermat. & Syph. **43**:42-61 (Jan.) 1941.

4. The carotene used in this study was contributed by the S. M. A. Corporation, Chagrin Falls, Ohio, and the vitamin A was supplied by Abbott Laboratories, North Chicago, Ill.

is of interest that the mother and her father, brother and sister had been the subjects of a report by Zeisler [5] in 1923 on the hereditary aspects of certain cases of pityriasis rubra pilaris (fig. 1). The eruption in each of our patients had its onset between the first and the second year of life and became more intense as the patient became older. Characteristically the lesions were less intense during the warm weather but never cleared entirely. All of these patients were in apparent good health and had always been so, and especially were free from any type of hepatic or gastrointestinal disease. The family diet had always been adequate according to accepted standards.

In each case the base lines for dark adaptation and the blood levels for vitamin A and carotene were established by preliminary testing. Certain members of the family were then given carotene for ingestion, while other members were given vitamin A. Institution of vitamin therapy was followed by repeated clinical observations of the effect on the lesions of the skin as well as by retesting of the dark adaptation thresholds and repeated determinations of the blood levels for carotene and vitamin A. No changes in diet were made, and no topical medication was employed. The patients were observed during the course of nearly two years,

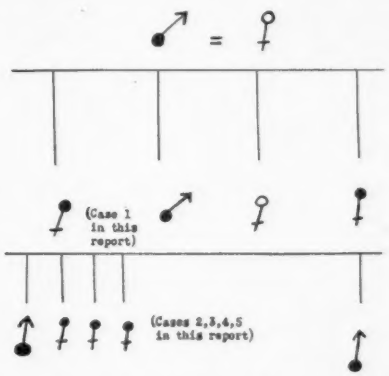

Fig. 1.—Hereditary aspects of pityriasis rubra pilaris in patients described herein. The dark symbols represent subjects in this family who were affected by the disease. The first two generations were previously described by Zeisler.[6]

in order to evaluate better the well known effects of warm and cold weather on the lesions of pityriasis rubra pilaris.

The biophotometer was employed in the determination of the dark adaptation throughout the course of this study. The technic recommended by Jeans, Blanchard and Zentmire [6] was utilized, and the complete curves for dark vision were plotted. Only the ten minute readings of the postrecovery period have been recorded in the accompanying charts.[7] The methods of Clausen and McCoord were used in the estimation of blood levels for carotene and vitamin A.[8] The deficiencies and limitations of these procedures were readily apparent as the study progressed and subsequently will be discussed in greater detail.

5. Zeisler, E. P.: Pityriasis Rubra Pilaris: Familial Type, Arch. Dermat. & Syph. **7**:195-206 (Feb.) 1923.

6. Jeans, P. C.; Blanchard, E., and Zentmire, Z.: Dark Adaptation and Vitamin A: A New Photometric Test, J. A. M. A. **108**:451-459 (Feb. 6) 1937.

7. Details of the results of studies of dark adaptation values for vitamin A and carotene in the blood appear in tabular form in the authors' reprints.

8. Clausen, S. W., and McCoord, A. B.: The Carotinoids and Vitamin A of the Blood, J. Pediat. **13**:635-650 (Nov.) 1938.

REPORT OF CASES [9]

CASE 1.—Mrs. W. H., a white woman aged 37, had an extensive eruption characteristic of pityriasis rubra pilaris and consisting of acuminate follicular plugging about the dorsal aspects of the hands and feet, and large plaquelike, scaling psoriasiform lesions of the extensor surfaces of the arms, legs and thighs as well as the neck and calves. There was also some involvement of the face, and the palms and soles presented the characteristic yellow, waxy appearance. There were numerous follicular keratoses of the extensor surfaces of the arms and thighs. The eruption was first noted when the patient was approximately a year old and had become increasingly more severe as she grew older. The lesions improved spontaneously in early summer but did not entirely disappear. This tendency to improve in warm weather was of considerable degree in the patient's youth but became less and less evident as she grew older. In recent years the eruption had been constantly and diffusely present summer and winter. A variety of local applications had been prescribed and used. Of these camphor ice rubs were the most effective. There had been no improvement after treatment with thyroid or with solution of potassium arsenite, but fractional roentgen therapy usually brought temporary relief. The general health was good.

Except for childhood diseases, the patient had had no significant infections. There had been no operations. There were no clinical or historical evidences of gastrointestinal disease. The patient did not ingest liquid petrolatum or other substances known to interfere with the absorption of vitamins. The diet was entirely adequate according to the ordinary standards. The general physical examination was essentially normal as were the routine urinary and hematologic studies.

Histologic examination of the skin disclosed the usual changes found in pityriasis rubra pilaris. There was diffuse hyperkeratosis with keratotic plugging of the follicles and spotty parakeratosis. The basal cells in some areas showed evidences of liquefaction degeneration. In the cutis a low grade nonspecific lymphocytic infiltrate with a tendency toward concentration above the blood vessels was observed. The sebaceous glands were found to be reduced in size and number.

The basic blood levels for carotene and vitamin A were found to be within normal limits. Preliminary dark adaptation tests showed increased thresholds. In May 1941 ingestion of carotene (50,000 equivalent units daily) was initiated.[9a] No obvious change in the cutaneous lesions resulted until about one month had elapsed. At this time generalized carotene discoloration was observed together with beginning disappearance of the follicular keratoses of the extensor aspects of the arms and legs. There was only slight effect on the plaquelike psoriasiform lesions or on the keratotic plugs of the dorsa of the hands and feet. Further treatment with the dosage of carotene increased to 70,000 equivalent units failed to produce significant improvement except for the disappearance of the follicular keratoses of the extensor aspects of the arms and thighs.

During the period of carotene ingestion, blood levels for this substance rose rapidly, virtually in direct proportion to the amount taken. There was no effect on the level for vitamin A. Significant lowering of the thresholds for dark adaptation did not occur.

In August 1941 vitamin A was substituted for the carotene. Doses of 100,000 to 200,000 units daily were given orally. Beneficial effects on the lesions of the skin were noted within a few weeks. The psoriasiform plaques became flattened and less erythematous and the keratotic plugging of the follicles on the dorsa of the hands and feet became softer and less prominent. With continuation of vitamin A therapy throughout the winter months there was further involution of the lesions of the skin. The former tendency of the eruption to recur with greater severity in this season was not observed. In February 1942 only faint erythema and slight scaling were present in the former sites of the large plaques. Almost no keratotic plugs were now observed about the dorsa of the hands and feet. Surprisingly, recurrence of the follicular keratoses of the extensor aspects of the arms and thighs was observed during this period of vitamin A treatment.

The blood levels for vitamin A increased in the course of this therapy and the former high value for carotene persisted, even though this substance was no longer administered. The results of tests for dark adaptation remained abnormal.

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9. These patients were presented at intervals in the course of this project at meetings of the Cincinnati Society of Dermatology and Syphilology.

9a. The preparations used were vitamin A capsules (Abbott), each furnishing 25,000 U. S. P. units of vitamin A derived from natural fish liver oils, and carotene capsules (Smaco), each furnishing 10,000 equivalent units and containing both alpha and beta carotene derived from vegetable oils.

In April 1942 all treatment was discontinued. Recurrence of the eruption, including the keratosis pilaris lesions, was observed within about four weeks. The exacerbation progressed until the usual beneficial effects associated with warm weather appeared. It was readily apparent, however, that the degree of this improvement was not comparable to that observed during treatment with vitamin A in the winter months. In October 1942 definite recurrence of the eruption was present. It was promptly controlled with administration of vitamin A. As previously noted, there was no effect on the keratosis pilaris. These lesions disappeared with addition of carotene (50,000 equivalent units daily) to the therapeutic regimen.

CASE 2.—W. H., a schoolboy aged 15, the eldest of 4 children, had a generalized classic eruption of pityriasis rubra pilaris which had been present in varying degrees since the first year of life. Large plaquelike areas of erythema, hyperkeratosis and follicular plugging were

Fig. 2.—*A*, pityriasis rubra pilaris and associated keratosis pilaris. *B*, involution of lesions following ingestion of vitamin A (case 2).

present about the extensor aspects of the forearms, hands, legs, thighs and feet (fig. 2*A*). Keratotic plugging was prominent about the dorsal surfaces of the fingers and toes. There was mild facial involvement, but the scalp was not affected. Moderately severe acne vulgaris was present. Follicular keratoses were numerous about the extensor aspects of the arms and thighs. The results of routine physical examination and laboratory studies were normal.

The patient's history was similar to that of his mother; the lesions had always shown some degree of spontaneous improvement during the warm weather; this phenomenon had become less evident as he grew older; the general health was excellent; the diet was adequate; past therapeutic response had been of temporary nature. The patient had previously been treated unsuccessfully by means of massive doses of vitamin D.

Preliminary studies of the dark adaptation revealed increased thresholds. The blood levels for carotene and vitamin A were within normal limits. Treatment was initiated in May 1941

with large doses of vitamin A (100,000 to 200,000 units daily). This treatment produced a rise in the blood levels for vitamin A without change in the values for carotene. No appreciable improvement in the response to dark adaptation tests could be determined. Clinically involution of the cutaneous lesions was observed within one month. The psoriasiform patches became less erythematous and less prominent, and the keratotic plugging about the dorsal aspects of the hands and feet showed evidences of involution. The follicular keratoses of the extensor aspects of the arms and thighs remained unchanged. After some three months of vitamin A therapy there was approximately 90 per cent regression of all lesions except for the keratosis pilaris lesions of the extensors (fig. *2 B*).

In July vitamin A treatment was discontinued and 30,000 to 50,000 equivalent units of carotene was ingested daily. The clinical improvement attained during the vitamin A phase of therapy continued for about two months, and there was rapid disappearance of the follicular keratoses of the extensor surfaces. There was steady progressive recurrence in most areas during the ensuing months, although the keratosis pilaris lesions of the extensor aspects of the arms and thighs did not reappear. The differences in therapeutic effect of vitamin A and carotene were readily apparent to the patient, and he pleaded for additional supplies of the former. The blood levels for carotene were strikingly increased during this experimental period, but there was no increase in the vitamin A level. The dark adaptation thresholds were not significantly affected, and remained abnormal (high) throughout.

In April 1942 all treatment was suspended, and the usual spontaneous improvement was observed in the warm weather which followed. The involution of the lesions during this period failed to approach that produced during the winter months by ingestion of vitamin A. Further treatment was now withheld until there was a moderately severe recurrence of the eruption with the onset of cold weather. At this time daily doses of 200,000 units of vitamin A were again administered. Beneficial effects on the lesions of the skin promptly occurred. It was of especial interest that the lesions of keratosis pilaris now disappeared, seemingly as a result of ingestion of vitamin A.

CASES 3, 4, and 5.—R. H., aged 13, P. H., aged 12, and E. H., aged 8, sisters of W. H., presented characteristic eruptions of pityriasis rubra pilaris. The lesions of these patients were of less severity (in direct proportion to the age) than in the aforementioned cases. No psoriasiform plaques were present. The eruptions consisted of hyperkeratotic plugs on the dorsa of the hands and feet, hyperkeratosis and plugging of the follicles about the knees and ankles and follicular keratosis of the extensor aspects of the arms and thighs.

The preliminary blood levels for vitamin A and carotene were normal in these patients, but the dark adaptation thresholds were for the most part abnormally elevated.

Generally the response to treatment with vitamin A and carotene paralleled that observed in cases 1 and 2. Ingesion of vitamin A produced elevation of the blood values for this substance (but not for carotene), and the reverse was true for the ingestion of carotene. The dark adaptation was not significantly affected by either medication, although occasional normal photometric readings were obtained without constant relationship to vitamin A or carotene therapy. Clinically there was usually improvement or disappearance of the follicular keratoses of the extensor surfaces with carotene, and slight or no effect on the other lesions. Vitamin A produced involution of the keratotic plugging on the hands and feet and of the hyperkeratotic patches about the knees and ankles, but did not affect the lesions of keratosis pilaris on the extensor surfaces of the extremities.

COMMENT

Limitations of Experimental Methods.—The method of Clausen and McCoord[8] employed in the determination of blood values for carotene and vitamin A has perhaps been superseded by the more accurate procedure which utilizes the photoelectric colorimeter.[10] Unfortunately, this equipment was not available to us when these experiments were undertaken. Clausen and McCoord readily admitted that great variations among single determinations occur with their analysis and that one reading is therefore of no value. Their investigations were nevertheless sufficiently precise to enable them to establish that the vitamin A content of normal human plasma reaches a constant level soon after birth and that while it is appreciably influenced by infections, hypothyroidism and other conditions, it is

10. Yudkin, S.: Estimation of Vitamin A and Carotene in Human Blood, Biochem. J. **35**:551-556 (April) 1941.

not affected by season. Steininger, Roberts and Brenner,[11] using Clausen and McCoord's analysis, found the level of vitamin A to be grossly related to the amount consumed in the diet as determined from the history. Their study also showed that a depletion of dietary vitamin A in human subjects resulted in lowering of blood levels for this substance and that administration of vitamin A promptly brought about immediate elevation, often above the normal value. There was no correlation between the blood levels and the response to biophotometric testing. Steininger, Roberts and Brenner concluded that blood values do not accurately reflect the body's stores of vitamin A. Baum and McCoord[12] also were unable to find correlation between the vitamin A content of the blood and the response to biophotometric tests.

The accuracy of dark adaptation thresholds as determined by the biophotometer has been debated repeatedly in the literature and need not be reviewed in great detail.[13] Most observers have been of the opinion that the use of this method generally results in inconsistent data because of the existence of the "training factor" concerned with its use and because the instrument must be calibrated frequently. A few investigators, on the contrary, believe the biophotometric method when properly employed to be a satisfactory, practical procedure.[14] The balance of the evidence is against this, however. Lack of correlation between blood levels for vitamin A and biophotometric dark adaptation tests is conceded by all observers.[15] Other methods for determining dark adaptation, as for example the various modifications of the adaptometer, have similarly been subject to adverse criticism and an altogether satisfactory and practical procedure has not yet been developed.[16] It should be stated, moreover, that although a relationship between dark adaptation and vitamin A deficiency undoubtedly exists, there is some question as to whether diminished ability to see in the dark is an early or late sign of deficiency.[17] Furthermore, it appears that there are other causes of night blindness—certain diseases of the eye and perhaps certain infectious or epidemic

11. Steininger, G.; Roberts, L. J., and Brenner, S.: Vitamin A in the Blood of Normal Adults: The Effect of a Depletion Diet on Blood Values and Biophotometer Readings, J. A. M. A. **113**:2381-2387 (Dec.) 1939.

12. Baum, W. S., and McCoord, A. B.: The Relationship Between Biophotometer Tests and the Vitamin A Content of the Blood of Children, J. Pediat. **16**:409-418 (April) 1940.

13. (*a*) Palmer, C. E., and Blumberg, H.: The Use of a Dark Adaptation Technique (Biophotometer) in the Measurement of Vitamin A Deficiency in Children, Pub. Health Rep. **52**:1402-1419 (Oct. 8) 1937. (*b*) Isaacs, B. L.; Jung, F. T., and Ivy, A. C.: Vitamin A Deficiency and Dark Adaptation, J. A. M. A. **111**:777-780 (Aug. 27) 1938. (*c*) Snelling, C. E.: The Biophotometer as a Test for Vitamin A Deficiency, J. Pediat. **13**:506-509 (Oct.) 1938. (*d*) Hecht, S., and Mandlebaum, J.: The Relation Between Vitamin A and Dark Adaptation, J. A. M. A. **112**:1910-1916 (May 13) 1939.

14. (*a*) Eckardt, R. E., and Johnson, L. V.: A Comparison of Two Methods of Measuring Dark Adaptation, J. Pediat. **18**:195-199 (Feb.) 1941. (*b*) Jeans, P. C.; Blanchard, E. L., and Satterthwaite, F. E.: Dark Adaptation and Vitamin A: Further Studies with the Biophotometer, ibid. **18**:170-194 (Feb.) 1941. (*c*) Dark Adaptation and Vitamin A, editorial, J. A. M. A. **117**:370 (Aug. 2) 1941.

15. (*a*) Caveness, H. L.; Satterfield, G. H., and Dann, W. J.: Correlation of the Results of the Biophotometer Test with the Vitamin A Content of Human Blood, Arch. Ophth. **25**:827-832 (May) 1941. (*b*) Baum and McCoord.[12] (*c*) Steininger, Roberts and Brenner.[11]

16. (*a*) Dann, W. J., and Yarbrough, M. E.: Dark Adaptometer Readings of Subjects on a Diet Deficient in Vitamin A, Arch. Ophth. **25**:833-838 (May) 1941. (*b*) Sloan, L. L.: Instruments and Technics for the Clinical Testing of Light Sense: I. Review of the Recent Literature, ibid. **21**:913-934 (June) 1939.

17. Kruse, H. D.: Medical Evaluation of Nutritional Status: IV. The Ocular Manifestations of Avitaminosis A, with Especial Consideration of the Detection of Early Changes in Biomicroscopy, Pub. Health Rep. **56**:1301-1324 (June 27) 1941.

conditions unrelated to deficiency of vitamin A. It is apparent that an appreciation of these facts is essential in the proper evaluation of the dark adaptation phase of this and similar studies.

In our patients with familial pityriasis rubra pilaris blood levels for carotene and vitamin A and photometric dark adaptation thresholds appeared to be of little significance. We regularly observed increased blood values following supplementary ingestion of carotene and vitamin A, and there was eventual return to the normal when treatment was no longer given. Some relationship between the content of carotene and vitamin A in the blood and the clinical efficacy of these substances was therefore necessarily present, but a complete lack of correlation with reference to blood values and photometric tests was found to exist. We were unable to demonstrate lowering of abnormal dark adaptation thresholds following therapeutic ingestion of either vitamin A or carotene. Among control subjects—supposedly normal persons chosen at random from hospital personnel—elevated thresholds were not uncommonly found. The existence of the "learning factor" was obvious among these persons and to a limited extent among our experimental subjects. Because of these facts we were unwilling to place much reliance on the dark adaptation readings as determined by the biophotometer.

Clinical Response to Treatment with Vitamin A and Carotene.—Our investigations with the vitamin A and carotene therapy of these patients with pityriasis rubra pilaris indicated that the cutaneous lesions were in general favorably influenced by this treatment. The psoriasiform plaques, the isolated guttate areas of hyperkeratosis and plugging of the follicles and the follicular keratotic plugging of the dorsa of the hands, feet, ankles and knees improved or completely disappeared within a few weeks to several months with ingestion of vitamin A in dosage of 100,000 to 200,000 units daily. Continuation of this treatment over a longer period usually resulted in virtually complete resolution with residual mild scaling and underlying dusky erythema alone remaining. Complete involution of all lesions was approached but not achieved in these subjects. Apparently the therapy must be continued indefinitely if recurrences are to be avoided. It appeared possible, however, that "sustaining" effect of some degree might have been accomplished in some instances when treatment was no longer given. Toxic effects from prolonged administration of relatively large doses of vitamin A and carotene were at no time observed in this study.

One of the most interesting observations was the usual failure of vitamin A to bring about involution of the follicular keratoses of the extensor aspects of the arms and thighs. Since keratosis pilaris lesions have been assumed to represent a classic manifestation of vitamin A deficiency, it was surprising that these lesions usually cleared with ingestion of carotene, and that (except in case 2) vitamin A was without effect.[18] In this regard we have investigated the effect of the ingestion of carotene on a limited number of patients with lesions of keratosis pilaris unassociated with pityriasis rubra pilaris. The results have in general been unimpressive, and the entire subject needs further study. The irregularity in the clinical response of keratosis pilaris to vitamin A has previously been commented on by O'Leary.[19] The explanation is not clear, but the numerous known and unknown factors in the absorption, conversion, storage and metabolism of vitamin A and carotene are probably in operation.

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18. Dr. Leon Goldman has observed a similar therapeutic effect following ingestion of carotene in a patient with pityriasis rubra pilaris.

19. O'Leary, P. A.: Vitamin Therapy in Dermatology and Syphilology, Arch. Dermat. & Syph. **46**:628-634 (Nov.) 1942.

As mentioned previously, Peck, Chargin and Sobotka [2] have postulated the belief that Darier's disease might represent a nevoid cutaneous condition wherein there exists an inability to absorb vitamin A or an inability to convert carotene (provitamin A) to vitamin A. A similar opinion was given by Sulzberger when he stated that "it is possible that nevoid anomalies and hereditary factors result in faulty utilization of dietary ingredients or vitamins." [20] These lines of reasoning might well be followed here in explanation of our therapeutic results with familial pityriasis rubra pilaris. The apparent good health of the patients, their adequate diets and the greater response to vitamin A than to carotene would thus point to an inability to convert carotene to vitamin A. That this was not a full explanation was indicated by the fact that vitamin A did not usually cause involution of the associated lesions of keratosis pilaris, whereas carotene as a rule was most effective in this respect. The existence of a "carotene deficiency" in these patients would offer a convenient though entirely hypothetic explanation.

Clinical response to vitamin A and carotene in the presence of normal original hematologic values for these substances was not especially disturbing. The analytic methods were admittedly crude, and, moreover, there need not necessarily exist a relationship between the concentration of a given substance (vitamin A) in the blood and the amounts present in the other tissues or the requirements of the tissues.[21] That the response to dark adaptation tests was not restored to normal by ingestion of vitamin A and its precursor was undoubtedly partially due to the insensitivity of the methods employed. These results were in distinct contrast to those of Brunsting and Sheard in patients with acquired pityriasis rubra pilaris, whose subnormal dark adaptation was promptly corrected by administration of vitamin A and other vitamins. This discrepancy very probably can be explained on the basis of the different methods of testing for dark adaptation employed in these two studies, but the possibility of a fundamental difference in the nature of abnormal dark adaptation in acquired and in congenital pityriasis rubra pilaris is nevertheless intriguing. Since the phenomenon has not heretofore been studied in familial pityriasis rubra pilaris, analysis of dark adaptation by other methods would be of considerable interest.

Finally, we do not believe that these studies necessarily support the concept of simple (dietary or absorption) avitaminosis A as the cause of pityriasis rubra pilaris. Certainly the results of blood analyses and dark adaptation tests were inconclusive in this regard, and from the clinical point of view our patients showed no evidence of deficiency of vitamin A or other vitamins. It seems more probable that the unquestionable and consistent clinical improvement observed in these patients after administration of vitamin A and carotene will eventually be explained on the basis of increased requirements for these substances or perhaps on the basis of other physiologic mechanisms as yet undetermined which are present in patients with pityriasis rubra pilaris.

SUMMARY AND CONCLUSIONS

The role of carotene and vitamin A in the causation and treatment of familial pityriasis rubra pilaris has been investigated in a two year study of 5 patients.

Biophotometric tests for dark adaptation and determination of the levels for vitamin A and carotene in the blood appeared to be of little significance in this

20. Sulzberger, M. B., in discussion on Brunsting and Sheard.[3c]

21. Kruse, H. D.: Handbook of Nutrition: XXIII. Medical Evaluation of Nutritional Status, J. A. M. A. **121**:669-677 (Feb. 27) 1943.

study, and no correlation between these factors was found to exist. The deficiencies and limitations of experimental methods are discussed.

Ingestion of vitamin A was found to bring about pronounced and consistent involution of the lesions of the skin characteristic of pityriasis rubra pilaris in this series of patients. Ingestion of carotene also produced therapeutic benefit, but this was of lesser degree. These effects were demonstrated to be independent of the spontaneous improvement known to occur in pityriasis rubra pilaris during warm weather.

For the most part vitamin A was ineffective as a therapeutic agent for the associated keratosis pilaris observed in our patients. Ingestion of carotene, on the contrary, usually resulted in rapid involution of the lesions. A satisfactory explanation for this difference is not apparent, and comparable results could not be produced in a small group of patients with keratosis pilaris unassociated with pityriasis rubra pilaris.

The results of our investigations are offered as additional indications of an interrelationship between pityriasis rubra pilaris and vitamin A metabolism. Evidence to substantiate the concept of simple dietary or absorption avitaminosis A as the cause of pityriasis rubra pilaris is lacking. There are numerous unknown factors concerning the metabolism of vitamin A and its relationship to certain diseases of the skin. Their subsequent elucidation should clarify the therapeutic effectiveness of vitamin A in pityriasis rubra pilaris.

The staff of the gastric laboratory of the Cincinnati General Hospital carried out the determinations for the blood values of vitamin A and carotene. Dr. Marion A. Blankenhorn and the department of internal medicine made possible the use of the biophotometer.

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BLOOD LEVEL AND EXCRETION OF ARSENIC FOLLOWING SINGLE INJECTIONS OF CLORARSEN

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Much has been written concerning the distribution of arsenic in tissues and its excretion after the injection of the several arsphenamines. Fewer data have been published on the blood levels, distribution in the tissues and excretion of arsenoxide. Most of the studies of arsenoxide have been made with reference to "massive dose" therapy. Though there was no reason to suppose that the excretion of clorarsen would differ from that of arsenoxide, it was thought proper that such studies should be made with this drug.

Clorarsen (3 amino-4-hydroxyphenyldichloroarsine hydrochloride) was used a decade and more ago for yaws. Its use in the treatment of syphilis and its toxicity were described in 1941 by Tompsett, Downs, McDermott and Webster.[1] Kampmeier and Henning [2] have also studied its effect in the treatment of acute syphilis and as an alternate drug to use for persons having untoward reactions to the arsphenamines or to arsenoxide.

This paper presents studies on blood levels of arsenic and its excretion after single injections of clorarsen, with some control studies on the use of arsenoxide and arsphenamines.

METHODS

Determinations of arsenic were made by the colorimetric method of Chaney and Magnuson.[3] Obviously, all reagents needed were tested to establish freedom from arsenic. Samples of blood from numbers of persons having had no arsenotherapy were tested and were found to be negative for arsenic by this method.

For the determination of blood levels of arsenic after one injection of clorarsen, arsenoxide and neoarsphenamine, samples were drawn at varying intervals after the injection, usually from five to fifteen minutes. Since the therapeutic dose of the arsphenamines contains so much more arsenic than does that of arsenoxide or clorarsen, neoarsphenamine was used in arsenic-equivalent doses to provide approximately the same arsenic content as that in the newer drugs. The higher blood level of arsenic in such instances met any theoretic objection that the dose of arsenoxide or clorarsen was too small to be demonstrated in the blood stream.

Determinations were made usually on whole blood, though in some cases the blood plasma also was studied. The spinal fluid was examined for arsenic in 2 patients treated with clorarsen.

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1. Tompsett, R. R.; Downs, W. G.; McDermott, W., and Webster, B.: The Use of Clorarsen in the Treatment of Syphilis, J. Pharmacol. & Exper. Therap. **73**:412 (Dec.) 1941.

2. Kampmeier, R. H., and Henning, H. B.: Treatment of Syphilis with Clorarsen, Am. J. Syph., Gonor. & Ven. Dis. **27**:208 (March) 1943.

3. Chaney, A. L., and Magnuson, H. J.: Colorimetric Microdetermination of Arsenic, Indust. & Engin. Chem. (Analyt. Ed.) **12**:691, 1940.

The excretion of arsenic after a single therapeutic injection of clorarsen and mapharsen was followed for six days after injection. The patients were admitted to the hospital for this study. A two day control period on the general ward diet was used before the arsenical preparation was administered. Urine and stools were examined for arsenic during this control period as well as during the days following treatment. Urine specimens for any twenty-four hour period were pooled. The same was true for stool specimens, which are recorded in grams of dried stool.

COMMENT

The results of study of the blood level of arsenic after 1 injection of clorarsen are shown in table 1. In 6 instances after the injection of 11.4 or 17.0 mg. of arsenic in the form of clorarsen, the demonstrable arsenic in the blood was 0.05 mg. per hundred cubic centimeters or less. In 1 case no arsenic could be

TABLE 1.—*Concentration of Arsenic in the Blood Stream After a Single Injection of the Arsenical Preparation*

			Amount of Arsenic Recovered in Blood *			Amount of Arsenic in Spinal Fluid *	
	Amount Injected			Plasma Concentration, Mg. per 100 Cc.	Whole Blood Concentration, Mg. per 100 Cc.		Spinal Fluid Concentration, Mg. per 100 Cc.
Cases	Dose, Gm.	Arsenic, Mg.	Time, Min.			Time, Min.	
Clorarsen							
1	0.067	17.0	15	<0.05	<0.05	..	.....
2	0.045	11.4	10	.....	<0.00	15	<0.05
3	0.067	17.0	10	.....	<0.05	..	.....
4	0.045	11.4	5	.....	<0.05	..	.....
5	0.045	11.4	10	.....	<0.05	10	<0.05
6	0.045	11.4	5	.....	<0.05	..	.....
7	0.045	11.4	5	.....	<0.05	..	.....
Mapharsen							
8	0.06	17.0	10	<0.05	<0.05	..	.....
9	0.04	11.4	5	.....	<0.05	..	.....
10	0.04	11.4	10	<0.05	<0.05	..	.....
11	0.06	17.0	5	<0.05	<0.05	..	.....
12	0.06	17.0	10	.....	<0.05	..	.....
Neoarsphenamine							
13	0.1	20.0	15	0.375	.....	..	.....
14	0.1	20.0	15	0.2	0.1	..	.....

* Since colorimetric readings for arsenic of less than 0.05 mg. per hundred cubic centimeters are inaccurate, the results are recorded as less than this amount.

found. The amounts of arsenic found in the spinal fluid in 2 cases, after ten minutes in 1 of them and after fifteen minutes in the other, were of the same order of magnitude.

The results were the same with arsenoxide as with clorarsen. (No difference was found in the arsenic content of plasma or of whole blood.) Neoarsphenamine in doses providing comparable amounts of arsenic as well as in therapeutic doses produced much higher levels of arsenic in the blood.

We were unable to find any reference in the literature to the arsenic content of the blood after single injections of arsenoxide. Kolls and Youmans[4] found that about three fourths of arsphenamine leaves the blood stream within a few minutes after injection, and that the remainder is rapidly reduced to traces

4. Kolls, A. C., and Youmans, J. B.: Quantitative Studies with Arsphenamine: II. Distribution and Excretion After Intravenous Injection, Bull. Johns Hopkins Hosp. **34**:181 (June) 1923.

which may persist for twenty-four hours at least. Magnuson and Raulston [5] found that though arsenoxide given in single doses disappeared rapidly from the blood stream, repeated doses soon gave a high level. They felt that the tissues probably reached a high saturation point and could not absorb more.

With 4 patients receiving clorarsen, the excretion of arsenic in the urine and feces was followed for six days. Similar determinations were made for a fifth patient after an injection of arsenoxide. The arsenic content of the doses employed for these 5 patients was 11.4 mg.

The percentage of injected arsenic excreted by the kidneys in six days for the 4 patients receiving clorarsen varied from 18.6 to 20.8. The patient receiving arsenoxide, excreted 22.6 per cent (table 2).

By the 4 patients who received clorarsen, 21.6 to 43.4 per cent of injected arsenic was excreted in the stools during the six day period. The latter figure was the highest of the four. It is of interest that this patient had four loose stools

TABLE 2.—*Arsenic Excretion in the Urine in a Six Day Period After a Single Injection of the Arsenical Preparation*

	Case 1 Clorarsen 0.045 Gm. (11.4 Mg. Arsenic)		Case 2 Clorarsen 0.045 Gm. (11.4 Mg. Arsenic)		Case 3 Clorarsen 0.045 Gm. (11.4 Mg. Arsenic)		Case 4 Clorarsen 0.045 Gm. (11.4 Mg. Arsenic)		Case 5 Mapharsen 0.04 Gm. (11.4 Mg. Arsenic)	
	Quantity of Urine, Cc.	Arsenic Excreted, Mg.	Quantity of Urine, Cc.	Arsenic Excreted, Mg.	Quantity of Urine, Cc.	Arsenic Excreted, Mg.	Quantity of Urine, Cc.	Arsenic Excreted, Mg.	Quantity of Urine, Cc.	Arsenic Excreted, Mg.
Before treatment										
1st day	1,950	0.078	255	0.020	1,120	0.028	2,165	0	2,250	0
2d day	2,400	0.048	588	0.051	700	0	1,740	0	1,640	0
After treatment										
1st day	1,660	1.13	1,253	1.284	1,530	1.300	700	1.581	1,400	1.470
2d day	2,325	0.465	525	0.348	1,350	0.523	1,970	0.147	875	0.262
3d day	2,100	0.2	710	0.158	870	0.172	2,025	0.100	1,600	0.320
4th day	4,000	0.2	1,200	0.218	1,020	0.255	1,975	0.197	1,475	0.295
5th day	1,475	0.12	1,165	0.168	1,175	0.095	1,390	0.070	1,825	0.182
6th day	.....	.....	1,020	0.051	940	0.035	1,845	0.045	1,150	0.058
Total arsenic excreted in urine.....		2.125		2.227		2.380		2.140		2.587
Total percentage of arsenic excreted in urine.....		18.6		19.5		20.8		18.7		22.6

on the day following the injection, 3.69 mg. of arsenic being excreted on that day. The 1 patient who received arsenoxide excreted 19.2 per cent of injected arsenic in the feces during the six day period (table 3).

Table 4 shows that the total amount of arsenic excreted in urine and feces in the six days following the injection varied from 41.1 to 62.1 per cent of that injected in the form of clorarsen. The largest elimination was that of the patient who had loose stools. The patient receiving arsenoxide excreted a total of 41.9 per cent of the arsenic injected.

Our results differ from reports on arsenic excretion following injection of single doses of arsenoxide. Gruhzit and Dixon [6] found that 65 to 95.5 per cent of injected mapharsen was excreted by dogs in one week after a single injection

5. Magnuson, H. J., and Raulston, B. O.: The Concentration of Arsenic in Tissues and the Excretion of Arsenic by Experimental Animals Following Intravenous Injection of Massive Doses of Mapharsen, Ann. Int. Med. **14**:2199 (June) 1941.

6. Gruhzit, O. M., and Dixon, R. S.: Mapharsen in Mass Treatment of Syphilis in a Clinic for Venereal Diseases, Arch. Dermat. & Syph. **34**:432 (Sept.) 1936.

of the drug. Foerster and his associates [7] studied the excretion of mapharsen by human beings. Four normal persons given 25 mg. of the drug excreted 64 to 78 per cent of the arsenic in six days. Nine syphilitic patients given 60 mg. of mapharsen excreted from 34 to 51 per cent of the injected arsenic in four days.

However, the differences may not be as significant as they appear to be. It must be noted that we used a different method for the determination of arsenic. The rate of arsenic excretion of lower animals is not necessarily the same as that of the human being. Foerster and his associates may have obtained a greater

TABLE 3.—*Arsenic Excretion in the Feces in a Six Day Period After a Single Injection of the Arsenical Preparation*

	Case 1 Clorarsen 0.045 Gm. (11.4 Mg. Arsenic)		Case 2 Clorarsen 0.045 Gm. (11.4 Mg. Arsenic)		Case 3 Clorarsen 0.045 Gm. (11.4 Mg. Arsenic)		Case 4 Clorarsen 0.045 Gm. (11.4 Mg. Arsenic)		Case 5 Mapharsen 0.04 Gm. (11.4 Mg. Arsenic)	
	Quantity of Feces, Gm. Dry Weight	Arsenic Excreted, Mg.	Quantity of Feces, Gm. Dry Weight	Arsenic Excreted, Mg.	Quantity of Feces, Gm. Dry Weight	Arsenic Excreted, Mg.	Quantity of Feces, Gm. Dry Weight	Arsenic Excreted, Mg.	Quantity of Feces, Gm. Dry Weight	Arsenic Excreted, Mg.
Before treatment										
1st day	42.5	0.037	19.3	0	16.7	0.033	29.4	0.015	12.6	0.006
2d day	....	.....	8.8	0	22.4	0	11.6	0.010	7.35	0.007
After treatment										
1st day	13.9	0.834	7.9	0.031	8.2	0.381	49.0	3.690	51.0	1.530
2d day	26.3	1.578	33.2	1.444	15.0	1.276	10.6	0.694	....	.....
3d day	32.8	0.639	13.2	0.697	26.3	0.565	8.1	0.470	17.2	0.017
4th day	37.8	0.277	17.85	0.192	21.5	0.301	....	.....	13.7	0.356
5th day	20.3	0.081	21.6	0.076	9.3	0.114	16.8	0.084	22.0	0.154
6th day	20.8	0.062	14.35	0.028	6.4	0.024	12.2	0.012	14.5	0.138
Total arsenic excreted in stool		3.471		2.468		2.661		4.950		2.195
Total percentage of arsenic excreted in stool		30.4		21.6		23.3		43.4		19.2

TABLE 4.—*Total Quantity and Percentage of Arsenic Excreted in the Urine and Feces in a Six Day Period After a Single Injection of the Arsenical Preparation*

	Case 1 Clorarsen 0.045 Gm. (11.4 Mg. Arsenic)	Case 2 Clorarsen 0.045 Gm. (11.4 Mg. Arsenic)	Case 3 Clorarsen 0.045 Gm. (11.4 Mg. Arsenic)	Case 4 Clorarsen 0.045 Gm. (11.4 Mg. Arsenic)	Case 5 Mapharsen 0.04 Gm. (11.4 Mg. Arsenic)
	Arsenic Excreted, Mg.	Arsenic Excreted, Mg.	Arsenic Excreted, Mg.	Arsenic Excreted, Mg.	Arsenic Excreted, Mg.
Total arsenic excreted	5.586	4.695	5.041	7.090	4.782
Total percentage of arsenic excreted	49.0	41.1	44.2	62.1	41.9

total excretion in six days based on a smaller amount injected, since there may be some threshold limit to the amount excreted at the beginning of the period. If this is the case it would not follow that a proportionate percentage of the injected dose would be excreted if larger doses were employed. On the other hand, for the syphilitic patients followed by Foerster and his associates for four days after the injection of 60 mg. of mapharsen, the results were similar to ours. Our figures are slightly higher for six days, the difference between our figures and those of Foerster no doubt being accounted for by the two extra days of diminishing excretion of arsenic.

7. Foerster, O. H.; McIntosh, R. L.; Weider, L. M.; Foerster, H. R., and Cooper, G. A.: Mapharsen in the Treatment of Syphilis, Arch. Dermat. & Syph. **32**:868 (Dec.) 1935.

Foerster and his associates found the proportion of arsenic excreted in urine and feces to be 1:1.65. In our cases the proportion varied from about 1:1 to 1:2. As was shown by the work of Kraft, Harris, Robinson and Gilliand [8] with rabbits, individual variations are so great that such values are probably of little significance.

SUMMARY

Clorarsen and mapharsen are removed from the blood stream so rapidly that practically no arsenic can be demonstrated after five to fifteen minutes. They differ from neoarsphenamine, traces of which may remain in the blood for as long as twenty-four hours.

Excretion of arsenic during a six day period following a single injection of clorarsen varied from 18.6 to 20.8 per cent in the urine and 21.6 to 43.4 per cent in the feces.

8. Kraft, R. M.; Harris, S.; Robinson, C. S., and Gilliand, H.: Quantitative Studies on Arsenic Distribution and Excretion After Intravenous Injections of Neoarsphenamine, Am. J. Syph., Gonor. & Ven. Dis. **22**:215 (March) 1938.

TREATMENT OF ACNE VULGARIS WITH COMEDOS BY MONOTERMINAL ELECTRODESICCATION

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Bloch,[1] in discussing the cause of acne, stated:

> It is well known that the development of a typical case of acne has two chronologically separate phases. The first is characterized by the formation of comedones. This (according to Unna) is caused by a thickening of the corneous layer at the outlet of and within the follicular duct, behind which the secretion of the sebaceous gland is blocked up. Only this phase of acne can be brought into direct relation with the endocrine processes in the sexual glands. The second phase of acne is characterized by an inflammatory and suppurative process on a basis of infection. . . . There is no consensus as to the actual cause of the infective inflammation.

If Bloch's thesis is correct, it logically follows that destruction of the comedos would prevent the pustular phase of acne vulgaris, and benefit greatly if not cure those with comedos and the second, or pustular, phase. In a recent symposium[2] on the treatment of acne, almost all the participants suggested therapy of the comedos, but no one suggested the possibility of destroying them permanently and thus, to all intents, "curing" the acne. It has been found possible to bring this result about by monopolar electrodesiccation of the comedos and the milia, with minimal scarring from the treatment. The scarring is much less than that caused by the normal progress of the acne.

Since use of the method was begun about two years ago, 83 patients with acne have been seen. Of this number 52 obtained favorable results from local therapy alone. The local treatment is essentially the same as that recommended in the symposium, except that no roentgen or special treatment of the comedos was used. The number of patients responding to local therapy only is in about the same percentage as was obtained in a previous study.[3] Thirty-one patients did not respond to the local efforts, and desiccation of the comedos was carried out, but 7 of these also received roentgen therapy locally.

The technic is simple. The ordinary spark gap machine is set so that a spark will jump about 1 mm. The small wall type of machine is set between the second and the third button. The amount of pain caused by the desiccation is tolerated easily by most people on the body, the forehead, the sides of the face and the chin, but the intensity may need to be decreased when one is working near the nose. Adolescents tolerate the pain less well than adults. The area is washed with 70 per cent alcohol and allowed to dry. A medium fine needle is inserted into the comedo or the milium to a distance of 1 to 3 mm. The current is then turned on with a foot switch and allowed to pass for from one to three seconds, the time depending on the size and depth of the comedo. The needle is then withdrawn and a spark is allowed to desiccate the surface for a fraction to one second. In

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1. Bloch, B.: Metabolism, Endocrine Glands and Skin Diseases with Special Reference to Acne Vulgaris and Xanthoma, Brit. J. Dermat. **43**:77, 1931.

2. Symposium on the Practical Management of Acne Vulgaris, J. Invest. Dermat. **3**:143, 1940.

3. Williams, G. E., and Nomland, R.: Gonadotropic Substance in the Treatment of Acne, J. A. M. A. **109**:564 (Aug. 21) 1937.

the case of double comedos, both openings are treated and the bridge between the openings is desiccated. Occasionally the bridge is cut with a scalpel and the entire lesion lightly desiccated.[4] A binocular loupe helps greatly because it magnifies and leaves both hands free.

The types of acne and the responses to treatment in 31 cases were as follows:

The first group of patients, consisting of adolescents ranging in age from 12 to 18 years (with a mean of 14 years), had ordinary mild to moderate acne with comedos, milia, papules and pustules, but no cystic lesions. Nine of the 11 received excellent results; 2 derived no benefit from the treatment, but had stopped after the first session of desiccation and must be classed as failures. No roentgen treatment was given to any in this group, and on their last office visit they were practically free of comedos.

The second group consisted of 9 patients, all but 1 of whom were women, whose ages varied from 22 to past 30. Most of these had oily skins, hypertrichosis and many superficial comedos. Seven received excellent results from the therapy. The man and 1 of the women did not benefit much. The woman in whom the treatment failed was the only one of the group that had received roentgen treatment.

The third group consisted of 6 males ranging in age from 14 to 22 years. They had pustular and mild cystic acne of the face only, with many comedos. All had considerable scarring from the previous acne lesions. Five of these benefited greatly and 1 only slightly. Three of them had concomitant roentgen treatment. One of the 3 who did not receive roentgen therapy had had this treatment previously; it had helped for a few months but was followed by a recurrence as severe as his original condition. He had one of the best responses to the desiccation treatment.

The fourth group consisted of 3 boys in their midteens who had severe acne of the face and body with severe pustular reactions, cystic lesions and large single and double comedos in all areas. All received weekly roentgen treatments (100 r a dose) for twelve weeks, in addition to the treatment of the comedos. Considering the severity of the acne and my previous lack of success in treating such cases, they all obtained excellent results.

Two patients with lesions of the acne conglobata type, in 1 widespread and in the other localized to the neck, derived no benefit from the combination of roentgen therapy and desiccation. Both of these men had deep cystic lesions and many double to quadruple comedos.

Of the 31 patients, only 6 had absolute or relative failure of treatment. For 3 of the persons for whom the treatment failed roentgen therapy was also used.

For patients like those in groups 1 and 2, with superficial lesions, the desiccation is minimal, of about one second's duration, and is essentially just a "buzz." There is little reaction, and the small crust falls off in about four days, leaving a red spot for about three weeks, after which practically no scars can be seen. For patients like those in groups 3 and 4, with large and double comedos, the duration of the desiccation may need to be maximal, about three seconds, and the reaction lasts longer. A scar results that is from 1 to 3 mm. across but is much less severe than the scar produced by the acne pustule. The scars on the face are smaller than those on the body. If the acne is limited to the face, from three to five sessions of fifteen minutes, at intervals of three weeks, suffice to destroy all of the comedos and milia.

4. Michelson, H. E.: Personal communication to the author.

SUMMARY AND CONCLUSIONS

Destruction of comedos and milia by monopolar electrodesiccation was carried out in 31 patients with various types of acne who had not responded to simple treatment. Excellent results followed in 25 patients. The best results were obtained in the mild acne of adolescents and in the superficial type seen mostly in women in their midtwenties.

Acne of the acne conglobata type did not respond, but patients with less severe eruptions had a good response, particularly when desiccation was combined with roentgen treatment, a method which was used for 7 patients.

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INCIDENCE OF PSORIASIS AMONG THE POPULATION AT LARGE

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How common is psoriasis among the general population? One searches the dermatologic literature in vain for an answer to this question. Yet more people have psoriasis than any other disease of the skin. Eczema, dermatophytosis and acne vulgaris outrank it in frequency at a dermatologic clinic, but none of these dermatoses lasts a lifetime. I have tried to determine the incidence of psoriasis in a crude way from the meager statistics available.

Psoriasis begins in about one-half the cases before the age of 20. The average age of patients with psoriasis at their first visit to a dermatologic clinic is, therefore, lower than that of persons with many dermatoses which appear in adult years, for example, herpes zoster and lupus erythematosus. Since there is no evidence that the life of a person suffering from psoriasis is shortened, it is not unreasonable to assume that his average expectation of life is at least thirty years from the time he makes his first visit to a dermatologic clinic.

At the Skin and Cancer Unit there are approximately 700 new cases of psoriasis annually. During the past six years, 1936 to 1941 inclusive, 873, 766, 692, 684, 695 and 665 cases respectively were observed there.

This means that there are probably no less than 20,000 persons with psoriasis alive to-day who have gone to the Skin and Cancer Unit at some time or other for treatment. Now, the Skin and Cancer Unit, although it is one of the largest dermatologic clinics in the city of New York, probably receives no more than 10 per cent of the total number of patients who go for treatment to the various clinics in the New York metropolitan area. Let it be assumed, however, that it receives as many as 20 per cent. This would indicate a minimum figure of 100,000 for the number of persons suffering from psoriasis in and around the city of New York, an area containing approximately 10,000,000. It should be noted that these statistics do not include the appreciable number of persons with psoriasis who have never gone to a dermatologic clinic for treatment, either because they have never consulted a physician or because they have always gone to their private physicians.

The conclusion is that not less than 1 per cent of the people living in and around New York are afflicted with psoriasis; the actual figure is probably considerably higher. Since there appears to be little difference between the incidence of the disease in New York and that in any other locality situated in a temperate climate and inhabited by the white race, I believe it is safe to say that at least 1 white person in every hundred has psoriasis.

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CHANGES IN THE FINGER NAILS IN PULMONARY TUBERCULOSIS

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Changes in the finger nails associated with chronic pulmonary tuberculosis have been observed and recorded since the time of Hippocrates. These include: (1) proximodistal incurvation, (2) clubbing, (3) pitting or depressions in the nail plate, (4) longitudinal or transverse ridging, (5) cyanosis of the nails and (6) disappearance of the lunula.

Hahn [1] published a statistical study on this subject in 1929. He found no hippocratic incurvation in normal controls, while it was present in 76 per cent of the patients with active tuberculosis, 50 per cent of the patients with inactive pulmonary tuberculosis and 30 per cent of the ex-patients working at his institution. Pittings and depressions in the finger nails were noted in all of his patients suffering from active pulmonary tuberculosis as compared with 6 per cent of patients in whom the disease had been inactive for a relatively short time; these changes were absent when the disease had been considered inactive for one year or longer. Cyanosis of the finger nails was observed by him in 66 per cent of patients with active pulmonary disease as against 2 per cent of those who had it in the inactive or chronic form.

Kaplan and Munson [2] studied the incidence of clubbing of the fingers associated with pulmonary tuberculosis in 426 patients of an average age of 47 years. They found 72 cases of varying degrees of clubbing, or 16.9 per cent. Analysis of the reports of other authors reveals a frequency of clubbing of from 20 to 21.7 per cent.

The only reference to changes in the lunula is found in the original work of Heller.[3] He stated that the lunula may disappear from the thumb nails during the course of pulmonary tuberculosis. Also, he expressed the opinion that the disappearance of the lunula from the thumb nails is an important diagnostic and prognostic sign. There is no information in the medical literature concerning changes in the appearance of the lunulae of the other fingers associated with diseases of the lungs. For this reason we have examined 202 patients with moderately advanced and far advanced pulmonary tuberculosis. Our interest in this subject was stimulated by the case of 1 of our patients from whose finger nails all the lunulae disappeared during the acute phase of a pulmonary abscess and reappeared again when he recovered.

The disappearance of the lunula is explained on the basis of an edema of the soft tissues of the distal phalanges. As the result of this localized edema there

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1. Hahn, A. G.: Studies on Changes in the Finger Nails in Pulmonary Tuberculosis, Am. Rev. Tuberc. **20**:876, 1929.

2. Kaplan, R. H., and Munson, L.: Clubbed Fingers in Pulmonary Tuberculosis, Am. Rev. Tuberc. **44**:439, 1941.

3. Heller, J.: Die Krankheiten der Nägel, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1927, vol. 13, pt. 2, p. 281.

develops a partial obstruction of circulation with dilatation of some of the blood vessels and an overgrowth of horn.

There were 67 patients with moderately advanced tuberculosis and 135 with far advanced tuberculosis in our group. Only male patients and controls were studied; we wanted to avoid alterations in the size and shape of the lunula caused by manicuring. One hundred healthy persons served as controls.

The average width of the lunulae in the controls and in various groups of patients is presented in table 1. The difference between the controls and the patients is obvious. On the right hand the lunula is 28.6 per cent smaller on the thumb in the tuberculous subjects than in the controls. Corresponding decreases in size of the lunulae are: second finger, 45 per cent; third finger, 52.9 per cent; fourth finger, 66 per cent; fifth finger, 63.6 per cent. On the left hand decreases in the average diameter of the lunula in the tuberculous subjects are: on the thumb, 30 per cent; on the second finger, 44.4 per cent; on the third finger, 62.5 per cent; on the fourth finger, 66.6 per cent, and on the fifth finger, 66.6 per cent. Measurements on patients with roentgenologically demonstrable formation of

TABLE 1.—*Average Width of Lunulae in Millimeters*

	Right Hand					Left Hand					Average of Both Hands				
	Fingers					Fingers					Fingers				
Persons Examined	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
Controls	3.5	2.0	1.7	1.1	0.4	4.0	1.8	1.6	0.9	0.3	3.7	1.9	1.2	1.0	0.3
Active pulmonary tuberculosis moderately advanced and far advanced	2.5	1.1	0.8	0.4	0.1	2.8	1.0	0.6	0.3	0.1	2.6	1.0	0.7	0.3	0.1
Pulmonary tuberculosis with formation of cavities	2.5	1.3	0.8	0.5	0.1	2.8	1.4	0.8	0.4	0.1	2.6	1.3	0.8	0.4	0.1
Pulmonary tuberculosis with clubbing of the fingers	2.3	1.2	1.0	0.4	0.0	2.5	1.2	0.7	0.4	0.1	2.4	1.2	0.8	0.4	0.0
Pulmonary tuberculosis with severe dyspnea	2.2	0.7	0.3	0.1	0.1	2.7	1.1	0.3	0.0	0.0	2.4	0.9	0.3	0.0	0.0
Silicosis with superimposed pulmonary tuberculosis	2.2	0.9	0.3	0.2	0.0	2.4	0.5	0.4	0.2	0.0	2.3	0.7	0.3	0.2	0.0

cavities showed no substantial deviation from figures obtained in the entire group. This indicates that a destructive, excavating type of tuberculosis is not in itself more liable to induce these changes in the lunula than parenchymal tuberculosis without cavity. On the other hand, it is interesting to note that in tuberculous patients with severe dyspnea there is a greater decrease in the size of the lunula than in patients without dyspnea. As compared with normal controls the decrease in the dyspneic group, expressed in percentage, on the right hand was: thumb, 37.1 per cent; second finger, 65 per cent; third finger, 82.2 per cent; fourth finger, 90.9 per cent, and fifth finger, 75 per cent. The decrease on the nails of the left hand was: on the thumb, 32.5 per cent; on the second finger, 38.8 per cent, and on the third finger, 81.2 per cent. On the fourth and fifth fingers the lunulae were absent. Practically identical reduction in the size of the lunulae was observed in patients whose pulmonary tuberculosis was superimposed on silicosis.

The maximum width of the lunulae in the controls and in various groups of tuberculous patients is given in table 2. One is impressed by the difference between the number of controls and of patients with moderately advanced and far advanced disease who come under the first subdivision, that is, in whom the sum of the maximum widths of the lunulae of all fingers of either hand measured

15 mm. and over. Relatively wide lunulae were seen in the controls 6.2 times more frequently than in patients on the right hand and 3.3 times more frequently on the left hand. Also, a significant difference was found in the frequency with which the lunulae were absent from all fingers, including the thumbs, in controls and patients. The lunulae were absent 4.2 times more often in patients than in

TABLE 2.—*Distribution of Cases According to the Sum of the Maximum Widths of the Lunulae of All Finger Nails, Including Those of the Thumbs*

Persons Examined	15 Mm. and Over		10-14 Mm.		5-9 Mm.		Less Than 5 Mm.		Absent from All Fingers	
	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent
A. Right Hand										
Controls	18	18.0	25	25.0	36	36.0	17	17.0	4	4.0
Active pulmonary tuberculosis, moderately advanced and far advanced	6	2.9	27	13.4	64	31.7	71	35.1	34	16.8
Pulmonary tuberculosis with formation of cavities	5	7.2	6	8.7	24	34.8	20	28.9	14	20.3
Pulmonary tuberculosis with clubbing of the fingers	2	4.0	8	16.0	11	22.0	19	38.0	10	20.0
Pulmonary tuberculosis with severe dyspnea	0	0.0	0	0.0	4	40.0	4	40.0	2	20.0
Silicosis with superimposed pulmonary tuberculosis	0	0.0	2	15.4	1	7.6	6	46.2	4	30.8
B. Left Hand										
Controls	15	15.0	27	27.0	30	30.0	26	26.0	2	2.0
Active pulmonary tuberculosis, moderately advanced and far advanced	9	4.5	22	10.9	69	34.1	71	35.1	31	15.3
Pulmonary tuberculosis with formation of cavities	5	7.2	9	13.0	23	33.3	20	28.9	12	17.2
Pulmonary tuberculosis with clubbing of the fingers	3	6.0	3	6.0	16	32.0	17	34.0	11	22.0
Pulmonary tuberculosis with severe dyspnea	0	0.0	0	0.0	3	30.0	6	60.0	1	10.0
Silicosis with superimposed pulmonary tuberculosis	0	0.0	1	7.6	3	23.1	4	30.8	5	38.5

	C. Average of Both Hands				
	15 Mm. and Over, per Cent	10-14 Mm., per Cent	5-9 Mm., per Cent	Less Than 5 Mm., per Cent	Absent from All Fingers, per Cent
Controls	16.5	26.0	33.0	21.5	3.0
Active pulmonary tuberculosis, moderately advanced and far advanced	3.7	12.2	32.9	35.1	16.0
Pulmonary tuberculosis with formation of cavities	7.2	10.9	34.0	28.9	18.9
Pulmonary tuberculosis with clubbing of the fingers	5.0	11.0	27.0	36.0	21.0
Pulmonary tuberculosis with severe dyspnea	0.0	0.0	35.0	50.0	15.0
Silicosis with superimposed pulmonary tuberculosis	0.0	11.5	15.4	38.5	34.6

controls from the nails of the right hand, and 7.6 times more often from the nails of the left hand. Patients who had severe dyspnea and those suffering from pulmonary tuberculosis superimposed on silicosis did not show lunulae measuring 15 mm. or more. The lunula was absent 5 times more frequently in very dyspneic patients than in the controls, and 11.5 times more frequently in patients with pulmonary tuberculosis superimposed on silicosis than in the controls.

In the entire group of tuberculous patients with lunulae absent from the right hand clubbing of the fingers was noted in 26.4 per cent; the corresponding figure

for the left hand was 25.6 per cent. In this same group of patients hippocratic finger nails were observed in 30.4 per cent. There were some instances in which the lunulae were absent from the thumb but were present on from one to four fingers; this abnormality was present on the right hand in 15 per cent and on the left hand in 11.4 per cent of patients without lunulae on the thumbs; 2 of these patients had clubbed fingers and 1 had hippocratic finger nails.

CONCLUSIONS

Observations on changes of the lunulae of the finger nails in 202 tuberculous patients are presented. It was found that there is a tendency to a decrease in the width and to complete disappearance of the lunula in patients with moderately advanced and far advanced pulmonary tuberculosis. The lunulae were absent from all finger nails five times more frequently in the patients than in the controls. Diminution in the size of the lunula was greatest in patients whose pulmonary tuberculosis was complicated by silicosis. In the latter group the lunulae were absent from all finger nails eleven times more frequently than in the controls.

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YELLOW DERMOGRAPHIA

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NEW ORLEANS

We have had occasion to observe a dermatologic entity which has received but scant attention. The condition of yellow dermographia (*ikterische Hautschrift*)[1] has not been described in the American literature, although some reports have occurred in the foreign literature.[2] In the case to be described we are dealing with an instance of dermographia and beginning jaundice, conditions which seem essential for the spontaneous development of this entity.

REPORT OF A CASE

On Sept. 15, 1939 a white man aged 23 presented himself at the office complaining of an unusual "nettle rash" which had been present for two days. The patient, who was above average intelligence, stated that the lesions resembled hives, but that the centers were yellow. Examination revealed that there was a diffuse urticaria involving the chest, abdomen and back and that there were sporadic hives on the extremities. The periphery of the lesions was erythematous, but the centers were strikingly yellow, almost canary yellow, and were easily distinguishable from the surrounding, nonicteric skin. The administration of 0.4 cc. of a 1:1,000 solution of epinephrine hydrochloride caused a fairly rapid subsidence of the wheals, the yellow disappearing *pari passu* with the red. The skin was dermographic, and when it was stroked firmly with the finger nail a ridge was raised which resembled hives in that there was a yellow streak sandwiched between two red borders. This reaction was repeatedly demonstrated throughout the course of the illness, which lasted until Oct. 8, 1939. At the first visit there was a suspicion of icterus on examination of the scleras, but this was not definite. Icteric indexes were taken and showed a gradual rise from 10 to an acme of 63 with a subsequent decline to normal. The urine was concentrated and showed small amounts of albumin and quantities of bile. A white cell count on September 17 revealed leukopenia (4,750 cells) with a normal differential white cell count. The stools were clay colored during the course of the disease, which was typical of acute catarrhal jaundice. After the acute illness had subsided, the dermographia persisted and was present when the patient was reexamined on March 8, 1943, but there was no yellowing and there have been no further outbreaks of hives.

Just as the urine is frequently bile stained before clinical jaundice can be detected, so in our case jaundice was seen in the wheals before the surrounding skin and sclera showed any icterus.

Schürer [1] attempted to explain the mechanism of yellow dermographia by saying that normally bile pigment goes through the cutaneous vessels slowly, and that during the acute dilatation of capillaries which occurs in dermographia there is a more rapid outflow of blood plasma, resulting in wheal formation. On the absorption of plasma the bile pigments remain in the skin. Our explanation of this phenomenon is rather that the plasma containing bile pigment, having passed through the capillaries, is disposed more superficially in the skin and hence is more readily seen.

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1. Schürer, J.: Ueber ikterische Hautschrift, Deutsche med. Wchnschr. **48**:593, 1922.

2. (*a*) Strassburger: Deutsches Arch. f. klin. Med. **125**:123, 1918. (*b*) Jadassohn, J.: Xanthomatoide Färbung von Hauteffloreszenzen bei Ikterus, Deutsche med. Wchnschr. **49**: 1544, 1923; cited by Schürer.[1]

There can be little doubt that the visibility of the bile pigment is due to the movement of plasma out of the capillaries and not to the mere presence of a wheal, for a wheal produced by saline solution is not associated with changes in color.

Studies by Krogh and Harrop [3] made with vital red have shown that normally this dye will not penetrate capillaries, but will penetrate experimentally dilated capillaries. Jadassohn [2b] reported a series of cases of jaundice following antisyphilitic therapy. In those instances when urticaria could be demonstrated yellow dermographia was also present.

On the basis of this work, Perutz and Adlersberg [4] have studied a series of jaundiced patients and produced wheals by means of physiologic solution of sodium chloride, histamine phosphate and morphine sulfate. Although the wheals caused by saline solution produced no change in color, these authors were able to show that with histamine or morphine gradations in color ranging from lemon yellow to definite brown could be produced, the color depending on the size of the wheal on one hand and the intensity of the jaundice on the other.

By the use of histamine we have been able to duplicate these authors' work. It is well to point out that the color of the wheal produced by saline solution does not differ from that of the contiguous skin. However, the entry of the needle into the skin was sufficient to cause a release of Lewis' H substance, and only at the point of insertion was there an increase in the yellow color.

A striking parallel to our case is offered in one reported by Strassburger, [2a] who observed an urticarial eruption in association with Weil's disease. In this instance again, the urticarial eruption was more intensely yellow than the surrounding skin.

SUMMARY

A case of yellow dermographia is described. There have been no similar instances reported in American literature.

It would seem that jaundice, latent or overt, and urticaria are essential for the development of this phenomenon.

The Tulane University of Louisiana, New Orleans.

3. Krogh, A., and Harrop, G. A.: Quelques remarques sur les stases et les oedemes, Compt. rend. Soc. de biol. **84**:325, 1921.

4. Perutz, A., and Adlersberg, D.: Untersuchungen über die Anreicherung von im Blute kreisenden Farbstoffen in Hautquaddeln, Klin. Wchnschr. **22**:942, 1923.

Correspondence

CHRONIC SCARRING PSEUDOFOLLICULITIS OF THE NEGRO BEARD

To the Editor:—An article appeared in the June 1943 issue of the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY by Dr. Hermann Pinkus entitled "Chronic Scarring Pseudofolliculitis of the Negro Beard." The author states "that a search of the literature revealed a strange absence of reference to this condition." I have (under the designation "folliculitis barbae traumatica") previously described the same disease as an extensive form of ingrown hair and not sycosis vulgaris, for which it is commonly mistaken (ARCH. DERMAT. & SYPH. **32**:237 [Aug.] 1935). I believe I was the first author—certainly the first in the American literature—to report this extremely common disease of the Negro beard.

SIGMUND S. GREENBAUM, M.D., Philadelphia.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

ISOLATION OF COCCIDIOIDES FROM SOIL AND RODENTS. C. W. EMMONS, Pub. Health Rep. **57**:109 (Jan. 23) 1942.

In the area near San Carlos, Ariz., Coccidioides has now been isolated from soil and from rodents but has not yet been isolated from a human being with the disease caused by this fungus. Small rodents appear to constitute an important natural reservoir of Coccidioides. This may explain, on the one hand, the presence of the spores of the fungus in wind-blown soil contaminated by infected animals and, on the other hand, the difficulty of isolating the fungus from soil in which it has a highly localized and spotty distribution.

A NEW BASE FOR THE PROTECTIVE OINTMENT FOR THE PREVENTION OF POISON IVY DERMATITIS. LOUIS SCHWARTZ, JOHN E. DUNN and F. H. GOLDMAN, Pub. Health Rep. **57**:578 (April 17) 1942.

The contention that sodium perborate can detoxify the active principle of poison ivy in an acetone-aqueous medium is confirmed.

There are presented and discussed two new formulas for sodium perborate ointment in which the sodium perborate will retain its oxygen for several weeks if kept in a closed container but will liberate it when exposed to perspiration or water.

CHAULMOOGRA OIL IN THE TREATMENT OF LEPROSY. G. W. MCCOY, Pub. Health Rep. **57**:1727 (Nov. 13) 1942.

There is a widespread belief that chaulmoogra oil and its derivatives are valuable specifically curative agents in the treatment of leprosy. A good review of the therapeutic results is given. The author cites the opinions of four special students of the disease who have had from eight to twenty years of experience in the treatment of leprosy and have concluded that chaulmoogra oil and its derivatives are of little value in the treatment of leprosy.

COCCIDIOIDOMYCOSIS IN WILD RODENTS: A METHOD OF DETERMINING THE EXTENT OF ENDEMIC AREAS. C. W. EMMONS, Pub. Health Rep. **58**:1 (Jan. 1) 1943.

Coccidioidomycosis was found in wild rodents in additional localities in Arizona. It was not found in an area examined in New Mexico. Rodents appear to constitute a natural reservoir of the disease, and the presence of susceptible species may explain the endemicity of coccidioidomycosis. It is suggested that examination and culture of the lungs from samples of the rodent population (particularly of species of Perognathus) offer a quick and dependable method of determining whether Coccidioides is present in a specific locality. This information may be of value in deciding whether unnecessary risk is involved in the concentration in certain areas of persons from nonendemic areas.

A PRACTICAL PLAN FOR THE TREATMENT OF SUPERFICIAL FUNGUS INFECTIONS. SAMUEL M. PECK and LOUIS SCHWARTZ, Pub. Health Rep. **58**:337 (Feb. 26) 1943.

A comprehensive plan for the treatment of dermatophytosis is outlined. There is also a discussion of the dermatophytids. Treatment of dermatophytosis of various regions of the body is discussed, as well as prophylaxis and sterilization of materials.

PECK, Washington, D. C.

MYCOSES OF THE FEET. A. DESFORGES, Union méd. du Canada **71**:940 (Sept.) 1942.

The author believes that dermatophytosis of the feet is as common in Canada as in the United States and that it is usually caused by Epidermophyton inguinale. Because the author feels that pathogenic fungi do not live in symbiosis with comestible fungi, treatment by means of a paste made of brewers' yeast is recommended. When the acute symptoms subside, compound ointment of benzoic acid (Whitfield's ointment) and later 1 per cent alcoholic tincture of iodine are used.

TWO CASES OF ORAL PHARYNGEAL LEISHMANIASIS TREATED WITH PENTAMIDINE. R. M. HUMPHREYS, Ann. Trop. Med. **36**:9 (June) 1942.

Two patients with oral pharyngeal leishmaniasis were treated with pentamidine (4:4'-diamidinodiphenoxypentane). The drug was given intravenously in daily doses of 100 to 200 mg. One patient was given a total of 8,500 mg. of the drug from May to September. There were no toxic effects, and both patients showed definite improvement. In 1 case the lesion seemed entirely healed.

VACCINATION AGAINST JERICHO BOIL. I. KATZENELLENBOGEN, Ann. Trop. Med. **36**:28 (June) 1942.

Vaccination against cutaneous leishmaniasis by the inoculation of virus directly from human lesions is an old procedure, and since the material used for the purpose is uncontrolled unpleasant results are occasionally produced from secondary infection. In areas where the disease is endemic attempts have been made to carry out prophylaxis on a large scale by inoculation of living cultures of Leishmania tropica. In this study an attempt was made to produce Jericho boil (Oriental sore) by the inoculation of leishmania bodies from the spleens of Syrian hamsters infected with Leishmania tropica or of cultures of Leishmania tropica. One hundred and sixty-seven persons were inoculated, 82 with leishmania bodies and 85 with cultures. Of these, 152 were followed up, and in 135 of them a lesion developed. The incubation period varied from two to eight weeks. In 7 subjects lesions developed remote from the site of inoculation; it is probable that these persons had been inoculated during the incubation period of a natural infection. The author believes that in endemic centers newcomers and residents hitherto uninfected should be inoculated. LAYMON, Minneapolis.

A PROSTHETIC ULCER OF THE MOUTH. H. T. SIMMONS, Brit. M. J. **1**:119 (Jan. 25) 1941.

Twelve cases of this benign tumor are reported, 2 in detail. Three of the patients were men, and 9 were women. All were edentulous and had worn their dentures for from five to twenty-six years. All the dentures fitted loosely. The ulcers are more common in the lower jaw than in the upper and are more common in women than in men. They usually occur in the sulcus part of the cheek or between the lip and gum. There are always two or more ridges which gradually slope away into normal tissues. Ulceration may exist deep in the ridges. Discomfort is present only during attacks of inflammation. Usually the patient presents himself after having discarded his denture, and the mechanical cause may not, therefore, be evident at once. The disease is usually chronic, and bleeding does not occur except with deep ulceration.

Treatment consists of excision of the ridges with the diathermy cutting loop and light coagulation of the base. Healing takes place in about one month with very little scarring. Fitting of new dentures is imperative, and their use should be deferred for about six months after the healing of the wound. One patient had previously been treated with an effective dose of radium element implanted. The ulcer was completely resistant.

PARESIS FOLLOWING HERPES ZOSTER. A. BARHAM CARTER and JOHN B. W. DUNLOP, Brit. M. J. **1**:234 (Feb. 15) 1941.

Two cases are reported of lower motor neuron paralysis following lumbar herpes zoster. The first patient was a widow aged 73 who had an attack of herpes zoster of the right leg two months prior to her first observation by the authors. After this attack she complained of pain and weakness of the leg, which "tended to give way on walking." The scars of a recent herpes zoster were present on the inner side of the right thigh and on the front of the leg in the distribution of the third and fourth lumbar roots. Cutaneous sensation to pinprick and cotton wool was slightly diminished in this area. The right quadriceps muscle was slightly wasted and its power diminished. The right knee jerk was absent. The plantar reflexes were flexor, and the abdominal reflexes were absent. A roentgenogram of the spine showed osteoarthritis and some osteoporosis of the thoracic and lumbar vertebrae. Gradually there was improvement in power and restoration of the knee jerk. Nine months after the onset of the eruption she had greatly improved except for slight weakness of the quadriceps muscle.

The second patient was a married woman aged 53 who was seen with typical herpes zoster of the front of the right thigh which spread to the inner side of the right leg. The lesions approximated the distribution of the third and fourth lumbar spinal segments. Spinal fluid obtained by lumbar puncture contained 38 lymphocytes per cubic millimeter and 0.05 per cent protein. Four days later the herpetic eruption began to heal. The pain was persistent, and she could not lift her right leg from the bed. There was almost complete loss of power

of the quadriceps with wasting. The right knee jerk was absent. Two weeks later she could just extend the knee and flex the thigh, and the cerebrospinal fluid showed 16 lymphocytes per cubic millimeter and 0.03 per cent protein. She still had some nocturnal neuralgia. The knee jerk was still absent. Three months later a lumbar puncture showed 8 lymphocytes per cubic millimeter with 0.032 per cent protein. The knee jerk had almost fully returned, and her muscular power was fair, although she required a stick for walking. One year after the illness she was symptomless, except that the leg tired easily and she had ½ inch (1.3 cm.) of wasting of the right quadriceps muscle with persistent scars of the eruption. The knee jerk was restored.

Carter and Dunlop suggest the probability that herpes zoster is essentially an acute posterior poliomyelitis involving the whole of the segmental sensory neuron, including the posterior root ganglions. They suggest that the finding of occasional inflammatory changes of the anterior horn is due to the spread of the virus from the posterior horn and explains the occasional occurrence of motor lesions.

OBSERVATIONS ON SOME NORMAL AND INJURIOUS EFFECTS OF COLD UPON THE SKIN AND UNDERLYING TISSUES: I. REACTIONS TO COLD AND INJURY OF NORMAL SKIN. THOMAS LEWIS, Brit. M. J. **2**:795 (Dec. 6) 1941.

This contribution by Sir Thomas Lewis is divided into three parts under the subtitles of: I. "Reactions to Cold and Injury of Normal Skin," II. "Chilblains and Allied Conditions," and III. "Frost-Bite." These are three Holme lectures delivered at University College Hospital and present fundamental physiologic principles in the typical brilliant, crystal-clear manner of Lewis.

The effect of cooling on the blood flow to the skin is greatest in those parts of the body which present a surface that is large in relation to their mass—obviously, the limbs. The extremities of the limbs, particularly the digits, cool the fastest. Next, the ears and nose cool most rapidly because they too have relatively large surfaces. The first effect is a reduction of blood flow through vasoconstriction, which is brought about through three separate reactions: first, local contraction as a direct response of the vessels to cold; second, immediate general vasoconstriction by reflex action through the central nervous system, which is transient; third, a persistent general vasoconstriction produced by a central nervous mechanism stimulated by the effect of cold venous blood in the general circulation.

The skin has a local defense mechanism against cold. When a finger is dipped into ice water it becomes painful at first, but shortly afterward the pain disappears and the finger feels more comfortable because of a rise in temperature due to a reaction of local vasodilatation. This alternation of constriction and dilatation is periodic, and the result is to raise appreciably the mean temperature of the digit. This type of vascular response also occurs when the skin of the face—especially of the ears, chin and nose—is cooled and depends on a local axon reflex. This is proved by the failure of the periodic rise of temperature in those fingers which have lost their nerve supply and consequently have lost this reflex.

Cold actually injures normal skin. This is corroborated by the evidence of several observations. First, the effect of this axon reflex in producing local vasodilatation is suggestive of the local release of H substance, which supports the idea of actual injury. Local pain and tenderness appear whether the fingers are rewarmed rapidly or slowly. Local tenderness persists long after the skin has become warm again. This is suggested as due to the release of vasodilator substances in the skin as a result of cellular damage, particularly in view of the fact that these substances are held in situ.

Those unusual patients in whom conspicuous wheals are produced as a result of local contact with cold, and who frequently suffer simultaneously from paroxysmal hemoglobinuria, are further evidence of the injurious effects of cold on the skin.

When a limb is cooled for a prolonged period, it becomes definitely swollen; the pulps of the fingers or toes are more tense than usual; there is pitting which involves the subcutaneous tissue as well as the skin, and there is an increase in the volume of the limb, which may amount to as much as 15 per cent. If several of the limbs, therefore, become cold for a prolonged time, as by immersion in sea water or other comparable exposure, a substantial amount of fluid may be lost from the circulation, and this reaction may thus account for or contribute to a state of circulatory collapse.

OBSERVATIONS ON SOME NORMAL AND INJURIOUS EFFECTS OF COLD UPON THE SKIN AND UNDERLYING TISSUES: II. CHILBLAINS AND ALLIED CONDITIONS. THOMAS LEWIS, Brit. M. J. **2**:837 (Dec. 13) 1941.

This is a discussion of chilblain, erythrocyanosis of the leg and trench foot. The chilblain affects particularly the dorsal surfaces of the phalanges, especially between the joints.

It appears as a red swelling, usually itching and hot. There are vasodilatation and edema. The redness gives place to a deep purple or reddish purple, with itching, soreness and pain. The swelling may remain or increase. The skin may even ulcerate. The inflammation tends to become indolent and heals slowly. The lesions are provoked by cold and not by frost. Those who have chilblains of the hands are usually young people whose hands, in winter and summer, are habitually cold and deeply colored.

Erythrocyanosis of the leg appears as a vascular discoloration over the front of the leg immediately above the ankle. The skin is purple and red, overtense and sometimes shiny. Edema may be great. The skin may break down and form ulceration which is indolent and heals slowly. This lesion appears in those whose limbs tend to persistent coldness.

Trench foot sometimes begins with pain and tenderness without apparent abnormality, except that the foot is usually cold, red or blue and swollen. When the patient is out of the cold the foot may be hot. In the more severe forms the skin may form ulcers and become necrotic or even gangrenous.

In the first World War trench foot appeared among men who stood and worked in the cold water and mud of the trenches for days and was responsible for thousands of casualties in the first winter. Infections complicated the lesions, although the long exposure to wet and cold was the responsible factor.

These three conditions are different manifestations of essentially the same process and result from prolonged action of cold. Their chief distinctions lie in their location and their manner of exposure. Chilblains come mostly on exposed hands and those parts that cool most profoundly. When they affect the foot they often display the areas of chief exposure and sharply define those parts of the foot which are unshod. Erythrocyanosis is particularly a woman's malady and has recently become more frequent. Its prevalence dates from the shortening of skirts and the use of thin stockings. In cases of trench foot it is the feet only which have long been wet and cold.

Microscopically the lesions of all three diseases show subacute or chronic inflammation.

Immersion in ice water for relatively short periods of time does not produce chilblain of the exposed fingers. It requires prolonged exposure to cold to produce the effect. Also, areas which have once suffered are especially prone to suffer again. In other words, prolonged and repeated exposures are usually required to produce the clinical picture. The only predisposing cause of chilblain and erythrocyanosis is a habitually defective circulation of the limbs which produces a fall of the temperature of the skin in circumstances in which normal circulation would preserve natural warmth. In other conditions in which the blood supply to the limbs is defective, such as syringomyelia, anterior poliomyelitis, acrocyanosis, Raynaud's disease and thromboangiitis, chilblains often occur. Wearing of tight footwear and strapping of the legs intensify the injury of long exposure to cold by interfering with the blood supply. The essence of treatment lies in the establishment of natural warmth by protecting the limbs from cold and from mechanical injury and by warming the trunk with extra clothing, by warm rooms and by confinement to bed.

OBSERVATIONS ON SOME NORMAL AND INJURIOUS EFFECTS OF COLD UPON THE SKIN AND UNDERLYING TISSUES: III. FROST-BITE. THOMAS LEWIS, Brit. M. J. **2**:869 (Dec. 20) 1941.

When skin is frozen the affected patch at once becomes pale, dull, opaque and yellowish. The formation of ice crystals in the skin is accompanied by a definite pricking sensation or by short stinging pain. The frozen skin forms a hard plaque with sharply defined edges, like an embedded coin. When the frost extends deeply the frozen tissues are solid and immovable.

The freezing point of the skin is about —1 C. (30.2 F.). Freezing begins with difficulty, but once started it spreads rapidly throughout all the chilled tissue and progresses the more quickly the lower the point to which preliminary cooling has been carried. Washing the skin encourages freezing, whereas leaving the skin unwashed discourages it. This is well known to Arctic explorers, who leave their skin unwashed.

Frostbite occurs only when the air is dry and the temperature low. The radiant heat of the sun protects against frostbite, but wind favors its occurrence. Natural frostbite occurs chiefly in those parts of the skin that are exposed and in those parts that cool most rapidly, i. e. the fingers, the ears and the nose, in the order stated. Frostbite of the feet is unusual because circulation is generally maintained active by walking, although tight covering will increase the chance of frostbite. Freezing of the feet while they are immersed in sea water can hardly occur, for the temperature of the water cannot fall below —1.9 C. (—28.58 F.), which is its own freezing point.

After freezing, hyperemia develops when the skin is thawed. A triple response is produced locally owing to the release of H substance from the injured cells of the skin. The severity of the effect, of course, depends on the duration and intensity of the freezing. It may extend to the degree of necrosis. Time itself, apart from its influence in increasing the area involved, is not a material factor in the damage.

In the treatment of frostbite, rubbing the frozen part is not recommended. Friction will tend to damage the skin and increase the reaction. It is preferable to induce slow thawing and to prevent the return of full circulation to the damaged tissues. In the case of a limb, its arteries may be compressed until thawing is complete. The compression should then be released gradually to allow the blood to return to the limb little by little. If in the process of warming pain becomes severe it can be moderated by cooling the part once more as the circulation returns to it. From this point on, the treatment of the lesions which follow freezing is fundamentally no different from that of lesions following burns. Essentially these subsequent reactions are due to injury to the tissues.

APPEL, Lynn, Mass.

A DEPRESSION-HYPOSEXUAL-ALOPECIA SYNDROME. C. ALLEN and C. CARLYLE-GALL, Brit. M. J. **2**:67 (July 18) 1942.

Allen and Carlyle-Gall report the case of a 33 year old man with complete alopecia, associated with deep depression. All hair-bearing areas except the axillas were denuded. Lack of sexual interest occurred simultaneously with the alopecia This was associated with a decrease in or absence of capacity to fulfil the sexual act. The authors call attention to the similarity of the condition in their case to Simmond's disease. Although they do not attempt to explain the cause of the syndrome, they suggest the possibility of an endocrine origin. However, they state, the cause of the damage to the glands is yet to be determined.

CERVICAL RIB AND HYPERHIDROSIS. E. D. TELFORD, Brit. M. J. **2**:96 (July 25) 1942.

The cervical rib syndrome is one of muscular weakness, pain and possible vasospastic phenomena. Hyperhidrosis is uncommon. Telford explains the excessive perspiration on the basis of irritation by the cervical rib of the sudomotor sympathetic fibers which run in the lowest trunk of the brachial plexus. Of 92 patients with cervical rib on whom Telford operated, 2 complained chiefly of profuse hyperhidrosis of the affected hand. In each case prompt and complete recovery followed surgical removal of the rib.

ECHOLS, New Orleans [ARCH. NEUROL. & PSYCHIAT.].

SKIN DISEASES IN WAR. R. T. BRAIN, Brit. M. J. **2**:760 (Dec. 26) 1942.

Infections of the skin account for the great majority of diseases of the skin in war. Brain believes that in the treatment of impetigo 100 to 150 mg. of ascorbic acid each day is a useful adjunct to therapy with local antiseptics. Sulfanilamide powder as a 5 per cent solution in glycerin is preferred to the ointment.

The use of lotions and pastes is desirable as a wartime means of conserving fats. For mycotic infections, Whitfield's ointment is recommended, and the socks and shoes are disinfected with solution of formaldehyde. Sulfur, rotenone and benzyl benzoate are all of value in the treatment of scabies.

Recent experiments have cast doubt on the necessity for sterilizing the outer garments and bedding in the treatment of scabies.

SCABIES TREATED WITH ONE APPLICATION OF BENZYL BENZOATE. JOHN R. GRAHAM, Brit. M. J. **1**:413 (April 3) 1943.

Basing his observation on approximately 1,000 cases of scabies, Graham has found that one treatment with a 25 per cent benzyl benzoate emulsion will cure scabies in over 99 per cent of cases.

Whenever possible, all members of the family were treated simultaneously. Disinfestation of clothing and bedding was found unnecessary. At the most, the omission of disinfestation of these fomites gave an increase of reinfestation of approximately 1 per cent. The technic is as follows:

After the establishment of the diagnosis by clinical and microscopic examination the patient is given a hot bath. The skin is then dried and painted from neck to soles with a 25 per cent benzyl benzoate emulsion (N. W. F.) by an attendant using a 2½ inch (6.35 cm.) paint brush and paying particular attention to such areas as the gluteal folds. The emulsion dries in from five to ten minutes, after which the patient dresses and reports back for a follow-up examination in one week.

Secondary infection is treated by the application of 2 per cent solution of gentian violet. Dermatitis never occurred with one treatment of the emulsion. The saving in time, personnel, transportation, wear and tear on clothing and cash amounts to a considerable factor in areas where scabies is endemic.

TREATMENT OF SCABIES BY T.E.T.M.S. T. M. CLAYTON, Brit. M. J. **1**:443 (April 10) 1943.

Clayton reports the results of treatment of scabies with tetraethylthiuram monosulphide (T.E.T.M.S.). Both a 25 per cent emulsion and a 5 per cent aqueous solution were moderately effective, although when the latter was used a mild dermatitis occurred in approximately 10 per cent of the subjects.

The author feels that routine sterilization of clothing and bedding is of little value.

PEDICULOSIS CAPITIS AND INTELLIGENCE IN W.A.A.F. RECRUITS. HENRY R. ROLLIN, Brit. M. J. **1**:475 (April 17) 1943.

Because of the interest in the question of the correlation of parasitic infestation with intelligence, Rollins gave standardized intelligence test to a group of 312 W.A.A.F. recruits with pediculosis capitis and compared the scores with those of a similar group of recruits who were found on initial examination to be uninfested.

There was a decided difference in the scores of the two groups, the lowest scores in all tests being made by persons in the infested group, which suggests that pediculosis capitis is more prevalent among the less intelligent recruits. SHAW, Chattanooga, Tenn.

HISTOPATHOLOGY OF MANTOUX REACTION AND ERYTHEMA NODOSUM. R. VISWANATHAN, Indian J. M. Research **30**:257 (April) 1942.

The author compared the histologic changes of the Mantoux reaction with those of erythema nodosum and found them strikingly similar.

The same cellular reaction, perivascular cuffing and arteriolar and capillary involvement with thrombus formation are seen in both. There is no definite evidence of tuberculoid structure in either. In 2 cases erythema nodosum developed three and five days after Mantoux tests were performed.

VISIBLE FORMS AND POSSIBLE LIFE CYCLE OF LYMPHOGRANULOMA VENEREUM VIRUS. WALDEMAR E. COUTTS, JUAN MARTINI, ISAAC BRIEVA, JACOBS LERVER and ANTHONY SARID, J. Trop. Med. **45**:137 (Sept. 15) 1942.

In most diseases caused by viruses structures called inclusion bodies are found in the cytoplasm or nuclei of various cells or lying free among cells. Most authors who have studied lymphogranuloma venereum believe that the inclusion bodies which are found are the virus of the disease. In lymphogranuloma venereum such bodies are always found in the cytoplasm of cells in two forms: (1) microforms, the dimensions of which are under 1 micron, and (2) macroforms. The authors found inclusion bodies in 95.8 per cent of the inguinal nodes in lymphogranuloma venereum, in 94.2 per cent of thirty-nine rectal strictures, in 95.5 per cent of 37 cases of esthiomene and in 88.8 per cent of 9 cases of elephantiasis penis et scroti. From studies with experimental inoculations and cultures of tissue the authors believe that these granulocorpuscles are living matter and that variations in size and other characteristics represent periods of the life cycle of a virus. LAYMON, Minneapolis.

Society Transactions

LOS ANGELES DERMATOLOGICAL SOCIETY

L. F. X. Wilhelm, M.D., *President*

A. Fletcher Hall, M.D., *Secretary*

Jan. 12, 1943

Pagetoid Epithelioma (Scrotum); Arsenical Keratoses (Palms and Soles). Presented by Dr. Nelson Paul Anderson.

F. L., a white man about 50 years of age, presents a sharply demarcated ovoid area of redness, scaling and slight superficial infiltration on the right side of his scrotum. Both palms and soles reveal small but definite punctate arsenical keratoses. He states that the scrotal lesion began about two to three years ago and has persisted ever since. He has had a total of five or six roentgen treatments to the affected area, with temporary improvement. There is no history of arsenical medication. About six or eight months ago he had a lesion removed from the right shoulder (superficial epithelioma?).

The Wassermann reaction of the blood was negative. A biopsy was performed elsewhere and is said to have revealed only chronic inflammation.

DISCUSSION

Dr. Kendal Frost: I agree with the diagnosis.

Dr. Maximilian E. Obermayer: I should like to ask on which clinical and histologic features of this case the diagnosis of pagetoid epithelioma is based.

Dr. Nelson Paul Anderson: I use the term "pagetoid" for certain superficial epitheliomas. On the scrotum it might be said to designate a peculiar type of superficial intraepidermal epithelioma which occurs especially on the genitalia, both male and female. In the literature, one man calls them Paget's disease and another Bowen's disease. This patient had a definite small infiltration present which on superficial examination could have been considered an eczematous process. The lesion has changed considerably since the first time I saw the patient. Tonight it shows practically no infiltration but presents a definite pearly border. I have not made a biopsy.

Dr. H. C. L. Lindsay: I should make a diagnosis of superficial epithelioma. This man has another lesion just beginning close to the first.

Dr. A. Fletcher Hall: I saw this patient before Dr. Anderson did. At the time I saw him, I could not make such a diagnosis as the one under which he is presented tonight; and I do not think I am astute enough to make it yet, unless it were shown by histologic section. At the time I saw him, there was more infiltration than there is now; there was no definite border, as there is now, and no individual papular elevations throughout the center of the lesion, which are visible tonight. Inasmuch as the whole area looked like a scar or possible morphea, I gave him a roentgen treatment, because roentgen rays had relieved the itching in the past. He had had a biopsy made within the year by a dermatologist in Oakland; so I did not go farther toward making a diagnosis but wrote to the physician who made the biopsy to get the slide. I have not heard from him.

Dr. Nelson Paul Anderson: I should like to comment again, not about the lesion itself but about the arsenical keratoses on the palms and soles. When these are present along with a peculiar intraepidermal type of epithelioma, such as this man presents on the scrotum, I cannot help but feel that arsenic has played a role in the production of this lesion. Incidentally, he had a similar lesion removed from one shoulder about a year ago in Omaha.

Cheilitis Solaris. Presented by Dr. Anker K. Jensen.

A 33 year old Mexican presents a severe scaling condition of the vermilion border of the lower lip with diffuse induration. This eruption has been present for the past twenty years, being much worse when exposed to sun and wind but better when protected from these elements. Biopsy on two occasions has shown no evidence that the lesion is malignant.

Treatment has consisted of administration of various ointments and lotions and lately of twelve weekly intramuscular injections of 1 cc. of bismuth subsalicylate in oil.

DISCUSSION

DR. CLEMENT COUNTER: I believe the appearance of this man's lip suggests another diagnosis, lupus erythematosus confined to the vermilion part of the lip.

DR. A. FLETCHER HALL: I wondered why this was presented as a case of cheilitis solaris. The fact that the lesion gets worse when in the sun but does not clear up when protected from the sun would indicate that the sun has something to do with it, but it might indicate that the sun is not the only factor. I should also entertain the possibility of lupus erythematosus of the lip.

DR. CHRIS HALLORAN: I favor the diagnosis of lupus erythematosus of the lip.

DR. NELSON PAUL ANDERSON: I remember seeing this patient at the White Memorial Clinic. I think the disease is cheilitis actinica or solaris. Against the diagnosis of lupus erythematosus is the fact that it is extremely uncommon for this disease to involve the lower lip unless there is some involvement of the true skin. This man's case stands as an example of an interesting group of cases of a disease that is encountered from time to time in Mexicans. It occurs in track workers, section hands, farm hands and the like. It is remarkable that it occurs in them, because they are relatively immune to the effects of sunlight elsewhere. Just why that should be is an interesting problem.

DR. PAUL ROST (by invitation): I agree with Dr. Anderson. I think it is cheilitis. It was often seen in the Alps. There a special ointment was available. Movie actors acquired the eruption in the high mountains when exposed to the sun. We applied this special ointment, and it cleared up.

DR. MAXIMILIAN E. OBERMAYER: I agree with the diagnosis of cheilitis. As a chronic inflammation of this type predisposes to malignant degeneration, it would seem advisable to protect his lip with a light-filtering ointment, e. g. one containing phenylsalicylate is satisfactory. Desensitization may also be tried by internal administration of quinine bisulfate or resorcin. At the present time experimental work is being carried out by Dr. Rothman at the University of Chicago concerning the light-protecting effect of paraaminobenzoic acid, which appears promising.

DR. SAMUEL AYRES: It is a peculiar tendency of this disease to occur in dark-skinned persons. I have seen many examples of it in Mexicans and several in Japanese patients. One would expect dark skin to be more resistant to light. I do not recall that I have ever seen the disease in a Negro. I should like to ask Dr. Obermayer if he thinks administration of paraaminobenzoic acid would be in order.

DR. H. C. L. LINDSAY: Nicotinic acid is protective against sensitivity to sunlight. It will often lessen susceptibility to the actinic action of the sun, even in lupus erythematosus. It is also helpful in building up the mucous membranes when nicotinic acid is lacking in the system.

DR. ANKER K. JENSEN: Biopsies that were made revealed nothing characteristic of lupus erythematosus.

A Case for Diagnosis (Parapsoriasis?). Presented by DR. NELSON PAUL ANDERSON.

Mrs. C. F. L., a 32 year old white woman, presents a pink to brownish pink squamous eruption involving the thighs, lower parts of the legs, outer aspects of the arms, chest and lower part of the abdomen.

She states that it began as a small scaly area on the leg below the knee six years ago. This disappeared and then recurred two years later, spreading until the time when she became pregnant. The eruption entirely disappeared in the latter half of pregnancy but had started to recur by the time she left the hospital, two weeks after delivery. At the present time the eruption is the worst that it has ever been. The onset of the eruption apparently was simultaneous with the onset of pulmonary tuberculosis, which occurred in 1938. Some benefit has followed treatment with ultraviolet radiation but, in general, there has been little or no response to any medication.

DISCUSSION

DR. CHRIS HALLORAN: This case impressed me as one of parapsoriasis.

DR. H. C. L. LINDSAY: I suggest the diagnosis of erythema annulare perstans.

DR. A. FLETCHER HALL: I agree with Dr. Halloran as far as the diagnosis is concerned, and I should like to see a trial made of vitamin A therapy, because in some cases chronic parapsoriasis will respond to this.

DR. NELSON PAUL ANDERSON: I have seen this patient on two other occasions. The first time I saw her I believed that she had tinea versicolor and thought that I would find fungi. I took many scrapings, but fungi were not found. The second time I saw her, the eruption had changed considerably. This eruption first appeared six years ago, its onset apparently coinciding with the onset of acute pulmonary tuberculosis. About three years ago she was seen by Dr. Ruben Nomland, of Iowa City. He made a diagnosis of psoriasis. I cannot believe now that it is psoriasis, nor have I been able to believe it at any time I have seen the patient, and yet two months ago when I saw her she had definite pitting of several finger nails. I think the diagnosis of parapsoriasis is correct. As for vitamin A, she has had one month of rather intensive vitamin A therapy, both internally and externally in ointment, and there has been little or no relief.

Pityriasis Lichenoides Acuta (Haberman), Not Varioliform. Presented by DR. MAXIMILIAN OBERMAYER.

L. S., a 54 year old man of American stock, was first seen on Oct. 9, 1942, when he presented a pruritic eruption on the trunk and extremities of a few weeks' duration. The lesions consisted of firm, shotlike, indurated papules of a dull reddish or waxy color, from 2 to 4 mm. in diameter, which were irregularly scattered over the aforementioned areas and resembled Cimex lectularius bites. This impression was intensified by the finding of small centrally located hemorrhagic crusts on top of some of the lesions and by their arrangement in pairs and in groups of three. A diagnosis of "bedbug bites" was made. The patient received the news sympathetically and recalled that the first lesions had appeared after an excursion in the mountains, with primitive conditions of shelter. He was advised to avail himself of the services of an exterminator, which he did. Two weeks later the patient returned with a new crop of lesions of a similar type, while the original ones were still present. In addition, an annular lesion 1.5 cm. in diameter which consisted of a firmly indurated border covered with fine scales and a pale somewhat depressed center was present on his left ankle.

Fungi were not found in the scales, and the Wassermann reaction of the blood was negative.

Four weeks later the lesions had increased in number; one indurated papule with a slightly scaling center was removed for biopsy. Microscopic examination showed a fine parakeratotic scale. The prickle cell layer was slightly acanthotic, and ballooning and hydropic degeneration due to edema were present. All through the edematous corium a massive inflammatory infiltrate consisting mainly of large numbers of lymphocytes was located around the dilated blood vessels and extended to the deeper portions of the cutis. The diagnosis was then changed to pityriasis lichenoides acuta, not varioliform.

Generalized ultraviolet irradiation was administered three times a week.

Under this regimen the dermatosis has considerably improved. Many of the lesions have completely disappeared without leaving any trace, while others have decreased in size, and only a few new elements have been observed. The hemogram was normal.

DISCUSSION

DR. KENDAL FROST: I have seen this patient several times with Dr. Obermayer. It is too bad he was not shown a month ago, before he began treatment with ultraviolet rays, because the lesions have subsided tremendously. I think any one who saw him at that time, although the eruption was not typical of acute parapsoriasis, would agree that it fitted into that picture.

DR. MAXIMILIAN E. OBERMAYER: I thought it worth while to present this case for the following reasons: First, the eruption is purely papular; none of the lesions has ever progressed to the varioliform stage; secondly, the papular eruption, which frequently resembles an early papular syphilid and which has therefore given rise to confusion with that disease, looks similar to Cimex lectularius bites in distribution as well as in appearance of the individual lesions. I agree with Dr. Newman that the features of the eruption do not conform with Haberman's pityriasis lichenoides et varioliformis acuta because of the absence of varioliform lesions. The diagnosis was made by exclusion. Cimex lectularius bites could be ruled out by the inefficacy of exterminating measures, the constant recurrences of the eruption and the histologic examination; a bite from Cimex lectularius would have shown an infiltrate composed principally of polymorphonuclear leukocytes. On the other hand, the eruption started to subside with ultraviolet therapy, and the microscopic features are compatible with those of Haberman's disease. I think that the assumption of an exclusively papular form of pityriasis lichenoides acuta is correct.

L. F. X. WILHELM, M.D., *President*

A. FLETCHER HALL, M.D., *Secretary*

Feb. 9, 1943

A Case for Diagnosis (Early Localized Scleroderma?). Presented by DR. MAXIMILIAN E. OBERMAYER.

H. G., a 21 year old white woman, complains of slight swelling and tenderness on the inner side of the lower third of the left leg which comes on at long and irregular intervals. For several years, possibly longer, the patient has been aware of a change in color of the affected areas.

At present, the skin in the aforementioned location appears slightly elevated and yellowish white, forming a plaque about 5 cm. in diameter, the borders of which fade imperceptibly into the surrounding skin. In the center of the changed area a dark brown macular lesion about 2 cm. in diameter is present, which shows white atrophic "specks" in irregular distribution which give it a mottled appearance. The consistency of the skin appears normal on palpation. The patient is in excellent general health.

A biopsy of tissue from the central pigmented area showed a hyperkeratotic stratum corneum and an atrophic stratum mucosum with absence of rete pegs. The basal layer was hyperpigmented. In the corium there was an overgrowth of the subpapillary blood vessels with a mild perivascular infiltrate of round cells and fibroblasts. The collagen tissue was highly cellular, but the individual bundles were smaller than normal. No sebaceous glands or hair follicles were seen, and the sweat gland elements appeared to be small. The histologic diagnosis was epidermal atrophy with hyperpigmentation and dermal fibrosis.

The pigmented lesion was treated by another physician about one year ago by means of applications of some acid.

DISCUSSION

DR. SAMUEL AYRES JR.: I am not willing to make a definite diagnosis except to say the lesion represents some sort of atrophic process. It is not exactly characteristic of morphea, and yet it approaches that more closely than anything else I can think of. The unusual feature is the pigmentation.

DR. SAUL ROBINSON: The interesting finding is the deep tenderness on palpation of a subcutaneous nodule. I think the lesion is probably associated with phlebitis or a vascular condition. It seems like an unusual erythema induratum to me.

DR. A. FLETCHER HALL: Are the episodes of tenderness or pain at all suggestive of a glomus type of tumor?

DR. MAXIMILIAN E. OBERMAYER: No. Tenderness is slight; only today the patient said that the tenderness and the swelling were pronounced, but palpation could still be performed without increasing the tenderness.

DR. A. FLETCHER HALL: My thought was of the possibility of a morphea-like reaction on the surface associated with a glomus type of tumor below.

DR. MAXIMILIAN E. OBERMAYER: I was unable to arrive at a diagnosis. I considered the early stage of localized scleroderma, a possibility which, however, was not confirmed by histologic study. The microscopic diagnosis was dermal fibrosis with collagen bundles smaller than normal and not larger, as would be expected in scleroderma. The epidermal atrophy shown in the section may well have been caused by applications of acid by another physician. The patient told me today that seven years ago her leg was broken at the ankle; this additional information corroborates Dr. Robinson's suggestion that the disorder may be secondary to changes in tissues other than the skin. However, a roentgenogram of the leg did not reveal anything abnormal.

Intraepidermal Epithelioma. Presented by DR. A. FLETCHER HALL.

P. C. S., a 73 year old white man, states that he has had "eczema" on his hands and the sides of his neck off and on since 1897, when he states he was "poisoned by bunting" which he was handling in the dry goods business; when he stopped the dry goods business some years ago, the eczema cleared, but the present illness remained as a scaly patch behind the left ear. About one year ago, a chiropractor applied a salve to this area which irritated the surface; it then remained elevated, warty and crusting until I first saw the patient, in April 1942. At that time the lower half of the left postauricular space was the site of a crusted verrucous plaque measuring about 15 by 25 mm., with well defined borders. A diagnosis of epithelioma with secondary infection was entertained. After application for one week

of compresses wet with water containing zinc and copper sulfates ("Alibour water"), the condition had improved to the point where it looked more like a neglected patch of seborrheic dermatitis. The patient was then given six weekly roentgen treatments to this area, which left the skin almost clear; there was an inactive patch on the posterior aspect of the lobe of the left ear which showed dilated plugged follicular openings suggestive of lupus erythematosus.

On Jan. 12, 1943 the patient returned, with the postauricular area smooth but dull red, fairly well demarcated and showing slightly elevated nodules; the area on the back of the ear lobe still showed plugged dilated follicular openings. No treatment has been applied other than boric acid compresses and boric acid ointment. He states that he has not ingested arsenic at any time.

The Wassermann, Eagle and Kline reactions were negative (Jan. 12, 1943). A biopsy slide is presented for examination.

DISCUSSION

DR. ANKER K. JENSEN: I agree with the diagnosis. I was glad to see the patient.

DR. CLEMENT COUNTER: This man presents an interesting type of epithelioma, the eradication of which probably will have to be done with cautery or electrodesiccation. Probably more destruction will be necessary to obtain a cure than the depth of the tumor would indicate.

DR. SAMUEL AYRES: I think the lesion is a benign superficial epithelioma. The slide I looked at showed some areas where the epitheliomatous process appeared to be in the corium. It is probably a basal cell type.

DR. H. P. JACOBSON: The clinical appearance of the lesion, together with the microscopic observations, leaves no room for questioning the diagnosis of a malignant neoplasm. The intraepithelial epitheliomas, unfortunately, are usually radioresistant. I fully agree with Dr. Counter that the indicated treatment is total destruction of the lesion, and the method of choice is wide excision of the lesion with the actual cautery.

DR. A. FLETCHER HALL: I presented the case because in it, as frequently happens in other cases of the same type, the lesion has gone through stages of looking like everything but an epithelioma before admitting of correct diagnosis. This has looked like lupus erythematosus and seborrheic dermatitis. After the case of a similar eruption on the scrotum that Dr. N. P. Anderson presented at the last meeting, I thought it would be interesting to present a little more obvious example of the same disease.

A Case for Diagnosis (Lupus Erythematosus?). Presented by DR. IRVING BANCROFT.

Mrs. M., a 47 year old white housewife, states that her present eruption began four months ago as a patch on the right side of the base of the neck, at a point where a chain rubbed against the skin. This was quickly followed by other lesions of similar nature; none have appeared in the last few weeks. The lesions have been severely pruritic.

She now shows scattered oval, erythematous, thickened, pruritic, slightly scaling patches over the exposed area of the neck.

The Wassermann reaction and the reaction to a patch test with the chain were negative. A biopsy slide is presented for examination.

DISCUSSION

DR. H. P. JACOBSON: I should like to make a diagnosis of lichen planus. While the distribution of the eruption is somewhat irregular, the shape and color of the individual lesions are highly suggestive of lichen planus. The microscopic picture is consistent with that diagnosis.

DR. SAUL ROBINSON: I agree with the diagnosis of hypertrophic lichen planus.

DR. SAMUEL AYRES JR.: I agree with the diagnosis of lichen planus.

DR. C. R. HALLORAN: Clinically this impressed me as lupus erythematosus. The lesions are on the exposed parts, and their structure clinically is that of lupus erythematosus. The changes observed at the biopsy, however, are not specific for lupus erythematosus, but they do not preclude that diagnosis. At the same time, while they are not specific for lichen planus, they also do not preclude that diagnosis.

DR. M. E. OBERMAYER: While clinically the eruption suggested lichen planus, some of the histologic features, such as follicular plugging and colliquative degeneration of the basal layer of the epidermis, were more indicative of lupus erythematosus; thus Dr. Halloran's suggestion appears to be good. If the eruption is lichen planus, it is certainly atypical.

DR. W. H. GOECKERMAN: Dr. Obermayer has expressed my idea.

DR. NELSON PAUL ANDERSON: I think this is a good case to observe and study clinically and histologically. Moses Scholtz's philosophical address on the dynamics of dermatology should be read. In this patient are found lesions which appear to some to be lichen planus and to others lupus erythematosus. Histologically the eruption is more suggestive of lichen planus than of lupus erythematosus, although here again there is nothing clearcut. It illustrates that the agent that produces lichen planus and the agent that produces lupus erythematosus can evoke somewhat similar responses in different persons.

Seborrheic Dermatitis of the Eyelids and Canities of the Eyelashes. Presented by DR. KENDAL FROST.

Miss R. G., a 26 year old white woman, complains of an irritation of the upper eyelids which has been present for about one year. About nine months ago, the upper eyelashes began to turn white, as did a few hairs of the eyebrows.

Examination reveals erythema with mild scaling of the upper eyelids; there is a moderate amount of scaling throughout the scalp. The upper eyelashes are white in patches. There is an occasional white hair in the eyebrows.

Salicylic acid, sulfur and oil of cade ointment have been used on the scalp, and 2 per cent ichthammol in zinc oxide ointment on the eyelids. Seventy-five roentgens of unfiltered roentgen rays was given to the eyelids on February 1 and February 9.

DISCUSSION

DR. SAUL ROBINSON: I agree with the diagnosis of seborrheic dermatitis of the eyelids. This is a remarkable picture of canities. I have never before seen canities of the eyelashes.

DR. SAMUEL AYRES JR.: I agree it is a remarkable case of loss of pigment of the eyelashes. I would try the effects of paraaminobenzoic acid or calcium pantothenate.

DR. A. FLETCHER HALL: I think that in addition to what Dr. Ayres has just suggested, a little more of the vitamin B complex should be given, and it may influence the eruption of the eyelids. I do not see why an ordinary seborrheic dermatitis of the eyelids would show so little improvement after two months' treatment with the ointment she has used and two roentgen treatments. Perhaps there is a riboflavin deficiency as well.

DR. H. C. L. LINDSAY: Have any cultures been made of the scales from the eyelids? Cocci and fungi may be missed sometimes when scales are examined hurriedly with the microscope.

DR. KENDAL FROST: I showed this patient because she is the first with canities of the eyelashes I have ever seen. She has white hairs in the eyebrows also, but she pulls them out herself. I do not know whether the lesions on the eyelids are seborrheic dermatitis or neurodermatitis. I will make scrapings of the eyelids in answer to Dr. Lindsay's question and will try the use of vitamins as suggested by Dr. Ayres.

NOTE.—Cultures of scrapings from the scaly patches on the eyelids did not grow spores or myceliums. The patient is taking 10 mg. of calcium pantothenate three times a day.

Arsenical Dermatitis with Superficial Epitheliomatosis. Presented by DRS. L. F. X. WILHELM and W. H. GOECKERMAN.

Mr. W. D. B., a 72 year old white man, has had arthritis for the past ten years. About ten years ago he was given intravenous injections and drops by mouth, beginning at 1 drop and increasing daily. He does not remember any other medication by mouth taken in drop form, although he has had several previous severe illnesses. For the past year erythematous lesions which do not heal have been appearing on the trunk. He had several fractional roentgen treatments for this eruption about a year ago.

He now presents scattered erythematous plaques with some scaling distributed over the chest and back. There are several with a raised pearly border.

He has had one roentgen treatment of 1,050 r applied to each of two lesions on the chest (Jan. 29, 1943).

DISCUSSION

DR. MAXIMILIAN E. OBERMAYER: This case was interesting for two reasons. It was a good example of multiple superficial erythematous basal cell epithelioma, and the predisposing effect of arsenic was evidenced by the presence of mottled hyperpigmentation on the trunk. The absence of arsenical keratoses confirms my previous experience that the two cutaneous manifestations from arsenic, hyperpigmentation and keratoses, are seldom simultaneously present.

DR. SAMUEL AYRES JR.: Did you say that mottled pigmentation is seldom seen with the keratoses? I agree with the diagnosis of arsenical superficial epithelioma probably of the basal cell type.

DR. NELSON PAUL ANDERSON: I think this case is instructive for several reasons: First, to those who still feel that arsenic does not produce superficial epitheliomas, here is a man who undoubtedly has had arsenic and yet he presents no keratoses of the palms and soles. One of the recent articles by Hamilton Montgomery argues that in only a certain per cent of these cases is the eruption due to arsenic, that in the others there is no history of ingestion of arsenic or arsenical keratoses. One can have benign superficial epitheliomas undoubtedly due to arsenic and yet no arsenical keratoses of the palms and soles. Finally, I do not believe that any of these lesions can be removed by radiation therapy without production of radiodermatitis. I think that solid carbon dioxide would be the best treatment. This is the only kind of epithelioma which one is justified in treating with this agent.

DR. L. F. X. WILHELM: We presented this patient especially for Dr. Anderson's benefit. I think you all remember a patient I presented a number of years ago, a physician whom I had followed about fifteen years. His lesions responded beautifully to roentgen therapy; 750 to 1,000 r to a lesion absolutely eradicated it. I followed him long enough afterward to know that there were no sequelae from the irradiation.

Photosensitization Dermatitis (Hydroa aestivale? Allergic Dermatitis?). Presented by DR. H. P. JACOBSON.

Mrs. E. W. S., a 21 year old white artist, states that there has been extensive allergy in her family. At the age of 8 months an eruption appeared on her face. A similar eruption has recurred every year, coming in June and subsiding the latter part of August, except one summer when she was on a strict diet.

The present attack had its inception in June 1942. She underwent extensive testing at the Naval Hospital in Philadelphia, but nothing significant was revealed. In December and January she received roentgen treatments which almost cleared the eruption completely, but it recurred as soon as she reached El Paso, Texas, and has been extending and progressing since.

There is now an extensive eruption involving the lips and chin and various parts of the face, forehead and upper eyelids. The eruption on the chin is most acute and consists of a fairly well marginated inflammatory erythema associated with vesiculation and oozing. Exposure to atmosphere produces great discomfort, smarting and burning and a sensation of puckering. The eruption on the forehead, eyelids and other parts of the face is erythematosquamous.

DISCUSSION

DR. SAUL ROBINSON: This is an interesting case because of the peculiar distribution of the eruption. From what I can gather, I do not believe that this woman has an allergic dermatosis or hydroa aestivale. The diagnosis that seems more probable to me is a functional dermatosis or exudative neurodermatitis. Excitement seems to make the condition worse. She has been moving around a bit lately on account of her husband's occupation.

DR. KENDAL FROST: I agree with Dr. Robinson. I should call it an atopic dermatitis of the face.

DR. H. C. L. LINDSAY: I agree with Dr. Robinson. He has called attention to the fact that this patient is highly neurotic.

DR. MAXIMILIAN OBERMAYER: To suggest a diagnosis of neurodermatitis merely because the patient shows signs of nervous instability does not seem justified. The recurrence of the dermatitis at the beginning of summer every year since the patient was born points to solar eczema. I suggest a study of the effect of the various wavelengths of sunlight on the patient's skin and an investigation for porphyria.

DR. SAMUEL AYRES JR.: I should like to point out the peculiar distribution of this eruption around the mouth, which I cannot reconcile with photosensitivity; one would expect to find some lesions on the backs of the arms, on the front of the legs and around the ears. It does not fit particularly the diagnosis of atopic dermatitis, although apparently that angle has not been adequately studied. The eruption began in infancy, and at times it has been more extensive than now. This would certainly suggest the reasonable possibility of its being atopic dermatitis, and I think the patient should be carefully tested with scratch tests, not only with foods but with Karaya gum, which is contained in some chewing gums, tooth paste and gelatins. A sensitivity to Karaya gum or a drug sensitivity of some sort might account for the eruption's being around her mouth; however, that would not explain the seasonal aspects.

DR. ROGERS F. WAKEFIELD: One thing that struck me about this case is interesting apart from the dermatologic aspects. Is this woman neurotic on account of the eruption, or has the eruption occurred on account of a neurosis? Since it dates back to 8 months of age, I cannot feel that it arises from a neurosis. It does not occur on the backs of the hands, although she spends much time out of doors, but I do not think that this rules out the possibility of photosensitivity. She states that there was one whole summer when she had no dermatitis on the face while on a strict diet, limited according to the intradermal tests she had. She tried the same diet the next summer and found that she was no longer sensitive to those same foods and that the results were unsatisfactory. However, I cannot agree that the cause is a psychoneurosis. I think that she has a definite sensitization, but because of the length of the history I doubt whether it was brought on by drugs.

DR. H. P. JACOBSON: The features particularly puzzling are, primarily, the question of diagnosis and, secondarily, the therapeutic management. This patient undoubtedly is an allergic person, but whether the presenting eruption is purely an allergic expression or whether there is an associated nervous element present is not at all certain. The seasonal recurrence in the summer months and the exacerbation on her present trip when she reached a warm, sunny climate would apparently suggest the possibility of photosensitization as an etiologic factor. The interesting feature in the history is that some three years ago, while she was on an extremely limited diet and without any topical applications or other treatment, the eruption cleared completely. On the other hand, complete allergic studies in the Naval Hospital failed to show evidence of sensitivity to any dietary elements.

Contact Dermatitis of the Eyelids of Undetermined Cause. Presented by DR. SAMUEL AYRES JR.

Mr. H. A., a white man, a pipe fitter of about 30 years of age, was first seen on July 21, 1942, with an eruption about the eyelids. According to the patient, the condition began about two months prior to this with swelling of the eyelids and a "pimple" at the outer canthus of the left eye, which was opened about two days after the onset. The eye has continued to be red and inflamed at various times in spite of various local medication. The patient later recalled that he had had two ulcers on the left eye attributable to irritation from the glare of a welder's arc. These ulcerations had healed entirely, however, six weeks prior to the onset of the present eruption.

At the time of the first visit, the eruption consisted of ill defined redness and slight swelling and scaling involving the upper and lower left eyelids, extending down to the cheek. The conjunctiva was not especially red. At the time of the patient's most recent visit, on Feb. 8, 1943, the eruption consisted of a moderate degree of redness and slight puffing, involving the lids of both eyes.

Patch tests were made with various medications which the patient had been using, and he gave a strongly positive reaction to metycaine hydrochloride and merthiolate. Seven other medications which were tested were negative. Patch tests have also been made with match heads, nickel, paper, grease which the patient handles, liquid soap, "dusceal," shaving cream, his wife's nail polish and other cosmetics, as well as scraping from the frames of his eyeglasses, printer's ink, zinc chromate and galvanized iron. Reactions to all of these tests have been negative.

Treatment has consisted of nine fractional doses of roentgen irradiation to the left eyelids, and five doses to the right eyelids, together with various types of bland local application, 10 per cent boric acid ointment, 5 per cent sulfathiazole ointment, 2 per cent yellow mercuric oxide ointment, 2 per cent colloidal sulfur ointment, 33 per cent naftex in a zinc oxide starch base and wet dressings of solution of aluminum acetate diluted 1 to 15. The eruption has improved almost to the point of complete clearness several times but has recurred suddenly to such an extent as strongly to suggest a contact dermatitis. The left eyelid has been affected the greater part of the time, but at times both eyelids are involved and occasionally only the right eyelid.

DISCUSSION

DR. MAXIMILIAN E. OBERMAYER: I cannot agree with the suggested diagnosis. An eruption which has a symmetric distribution, fades imperceptibly into the surrounding skin and has never been accompanied by pruritus is not due to contact sensitivity but is of internal origin. As the absence of pruritus rules out the possibility of neurodermatitis, I suggest investigation as to sensitivity to phenolphthalein, which is not infrequently responsible for a chronic current nonpruritic eruption around the eyes.

DR. SAUL ROBINSON: I agree with Dr. Obermayer. I should like to see what would happen if this patient received some phenolphthalein internally.

DR. SAMUEL AYRES JR.: May I correct a point? I should like to call attention to the fact that this eruption has not been symmetric. Generally only the left eyelid breaks out. When that clears up, the other eyelid breaks out; and sometimes both break out simultaneously.

DR. A. FLETCHER HALL: I do not see why this cannot be a factitial contact dermatitis, and I think it is either that or a neurodermatitis. In questioning this man it is difficult to get him off the subject of the two physicians to whom his employer sent him and with whom he was dissatisfied; he harkens back to that frequently. The way he stands while talking and his whole attitude would indicate to me a good background of neurodermatitis or factitial dermatitis. He knows that he is sensitive to merthiolate and may be continuing its use surreptitiously, hoping to discredit the physicians whom he dislikes. I think it is a possibility not to be overlooked, even though he has never stopped working.

DR. H. C. L. LINDSAY: In dealing with similar eruptions, I always scrape some scales off the eyelids. Sometimes fungus is discovered microscopically or culturally. If it is due to fungus, the dermatitis will not disappear until the fungus is eradicated.

DR. WILLIAM H. GOECKERMAN: Some years ago Osburn tried to attribute a large percentage of such eruptions to nail polish and/or remover. In my experience I cannot corroborate his findings. I think, as Dr. Frost has pointed out, that each case presents individual problems under several different diagnoses. One always has the problem individually. At first I thought this man was using something internally that caused the flare-ups, but after observing his personality I should make a diagnosis of neurodermatitis. He is a peculiar person.

DR. SAMUEL AYRES JR.: This patient has presented a problem, and apparently the onset of his trouble consisted of several small ulcers on the cornea attributed to irritation from arc welding glare. Then a dermatitis and irritation around the eyes developed, which have gone on ever since. The old medication was discontinued when it was found to be irritating. First one eye is affected, then the other and then both. At times he has been almost well, with only a slight redness at the corner of one eye; then use of a 5 per cent yellow oxide of mercury ointment has caused the eruption to flare up again, although the result of the patch test was negative. As far as I can make out, he is not taking anything internally.

Multiple Extensive Ulcerations of the Legs. Presented by DR. SAMUEL AYRES JR.

E. G., a 55 year old white man, admits having had a genital lesion many years ago and states that he has suffered from arthritis involving nearly all of the joints during the past ten years. He dates the onset of his trouble to an ulcer which appeared on the left leg May 17, 1942, after he had struck his leg against a sharp corner. Additional ulcers began to appear after several months, and the patient was hospitalized. Injections were made into some varicose veins. Still more ulcers followed. Under the assumption that he had blastomycosis, the patient was given potassium iodide and sulfathiazole by mouth and local applications of powdered sulfathiazole. He was also given bromides while in the hospital, but he has received none since Oct. 3, 1942.

The patient is an undernourished-appearing man, past middle life. At the time of his first visit, on October 30, he presented extensive small and large ulcers covering all aspects of both legs and thighs and reaching almost to the buttocks. The newer lesions were brightly inflamed and pustular; the older ones consisted of large, sharply defined, circinate, necrotic granulating ulcers bathed in thick pus.

The patient was hospitalized, and wet dressings of water containing zinc and copper sulfate (Alibour water) and 2 per cent aqueous solution of gentian violet were applied. Later, chloriohydroxyquinoline ointment was used locally, autogenous vaccine containing Staphylococcus albus intravenously, and, in view of the probable former syphilitic history, thio-bismol intramuscularly. He was discharged from the hospital on December 19, with the lesions approximately 99 per cent well. However, at this time intolerance to the chlorohydroxyquinoline ointment developed, which necessitated its discontinuance.

Since then, some of the ulcers have recurred, and in one or two of the lesions on the thighs have developed what at first resembled furuncles. These became somewhat sluggish, and the characteristic ulcers which were present at the time of his first visit did not develop. Use of the vaccine and thio-bismol have been continued, and during the past two weeks the patient has received two intravenous injections of mapharsen of 30 and 40 mg. respectively. Locally he has applied tyrothrycin (gramicidin) in an oxycholesterol-petrolatum base (20 mg. per hundred grams). Between Jan. 8 and Jan. 25, 1943, some of the lesions had healed but there was still some activity present, and use of 5 per cent sulfathiazole ointment was begun at that time. At the present time, most of the ulcers are healed but there are a

few lesions ranging from pea to dollar size which are granulating and in places papilliform ulcerations with extensive scarring from former lesions.

The Kahn and Kline reactions were negative. Cultures on Sabouraud's medium and on Rosenow's brain broth revealed only Staph. albus. Smears revealed only gram-positive cocci. A routine examination of the urine revealed no abnormalities.

DISCUSSION

DR. H. P. JACOBSON: This patient presents a number of variously sized and shaped atrophic scars associated with a number of gummatous ulcerations in various stages of evolution. The eruption is of several years' duration. The morphologic picture, together with the clinical history, is consistent with a diagnosis of tertiary syphilis. His negative serologic reactions could possibly be accounted for on the basis of chronic alcoholism. The patient admits he has been a fairly heavy drinker, and his abstinence from alcohol is of rather short duration.

DR. CHRIS R. HALLORAN: The infectious granulomas are to be excluded, also pyoderma gangraenosum. However, the man impressed me as having bromoderma or iododerma.

DR. SAUL ROBINSON: I agree with the diagnosis of tertiary syphilis. I think the entire picture is probably due to a so-called lowered resistance to Spirochaeta pallida. I believe this patient's lesions would have cleared up with the older therapy, with arsphenamine and fever treatment. A patient at the Los Angeles County Hospital with a gumma of the nose responded to that therapy, and it would probably be worth while to use the same kind of treatment in this case.

DR. WILLIAM H. GOECKERMAN: I think a fair amount of work has been done, but today the disease is in a stage in which I do not believe one can see the real picture the patient would present untreated. However, there is a history, as far as I could get it, that after new lesions appear they are pustular. The man tried to tell me that a certain lesion on the leg oozed a lot of pus. I, too, felt that the disease was either bromoderma or iododerma. It would probably have to be observed in its various phases before one could strongly favor a definite diagnosis.

DR. KENDAL FROST: I agree with Dr. Halloran and Dr. Goeckerman. A late syphiloderm is almost always asymmetric. The peculiar papillomatous character of some of these lesions did not fit my conception of a syphilitic lesion. The lesion on his hip was inflammatory. There was a punched-out ulcer with a fairly acute erythematous halo. It had evidently started as a superficial lesion. It suggested more the diagnosis of bromoderma or iododerma than of a syphilitic lesion.

CHICAGO DERMATOLOGICAL SOCIETY

UDO J. WILE, M.D., *President*

MICHAEL H. EBERT, M.D., *Secretary*

Dec. 16, 1942

A Case for Diagnosis (Lymphoblastoma? Psoriasis?). Presented by DR. MICHAEL H. EBERT.

E. G., a Negro woman, states that eight years ago pea-sized, slightly scaly erythematous lesions which were slightly pruritic, developed on the dorsum of the right hand. In the interval of three years, similar lesions appeared elsewhere on the face, neck and body, and on all the extremities. These persistent lesions are getting larger with time, and off and on the patient has noticed easily removed dry grayish scales. She states that she has not used any internal medication except in 1925, when she received three injections in an arm and three in a hip "for her blood."

The patient reveals a generalized bizarre eruption with pea-sized to palm-sized polycyclic-bordered, velvety-appearing, depigmented to erythematous and noninfiltrated to moderately infiltrated lesions. There are a few pinpoint depressions on the left thumbnail.

Examination showed a hemoglobin content of 50 per cent, erythrocytes, 5,180,000 and leukocytes 7,600, with a differential count of 60 per cent polymorphonuclears, 27 per cent lymphocytes, 7 per cent monocytes, 4 per cent eosinophils and 2 per cent basophils. Chemical examination of the blood gave essentially normal results. The Kahn and Wassermann reactions were negative. The urine was essentially normal. Specimens were removed from one of the earliest lesions and from the most recent.

Histologic examination showed that the principal changes were in the epidermis. There were some hyperkeratosis and patchy parakeratosis. The granular layer was well preserved in places and absent in others. There was acanthosis of the rete but no corresponding elongation of the papillae, which did not approach closely to the surface. There was some migration of leukocytes and occasional accumulation of round cells under the stratum corneum. There was a slight round cell infiltrate about the vessels in the upper part of the corium.

NOTE.—A sternal puncture was performed later. There was no pathologic alteration in the cells.

DISCUSSION

DR. CLARK W. FINNERUD: I can only state an impression about which I do not feel certain. Clinically, from the character of these sharply demarcated lesions, I thought the eruption might be mycosis fungoides. I understand that the blood was found to be normal. I have seen early lesions of mycosis fungoides in the premycotic stage that showed no more cellular infiltration or variety of infiltrating cells than are present in these sections. The epidermal change, distinctly psoriasiform, was compatible with early mycosis fungoides. There were minute abscesses beneath the stratum corneum which fit in with the picture of the premycotic stage. The patient stated that there had always been considerable itching.

DR. M. J. REUTER, Milwaukee: The microscopic section was suggestive of psoriasis. However, this did not fit into the clinical picture, which was most unusual. The history, I believe, stated that there had been no disappearance of the lesions since the onset.

DR. M. H. EBERT: From the time this patient was in the wards of the Cook County Hospital her disease has presented a diagnostic puzzle, and after we got the sections it still presented a puzzle. When I saw her, my first impression was that perhaps it was some bizarre type of lichen planus. The biopsy ruled that out at once. I think these sections at first glance suggest psoriasis, but they are really not a good picture of active psoriasis. I should expect the papillae to approach the surface more closely. Perhaps Dr. Finnerud's diagnosis is the most rational one. An absolute diagnosis will have to await further observation.

A Case for Diagnosis (Schamberg's Progressive Pigmentary Dermatosis? Hypostatic Purpura?). Presented by DR. H. RATTNER and DR. M. DORNE.

Mrs. F. F., aged 65, presents an eruption of numerous pinhead-sized brownish macular lesions involving the feet, legs and lower portion of the thighs. The first lesions appeared on the feet three years ago; new ones continue to appear, the eruption spreading upward on the legs and thighs. The lesions do not disappear on diascopic pressure. There are no subjective symptoms. The patient has diabetes. She receives injections of insulin regularly, and sugar appears in her urine intermittently. Her right breast was amputated two years ago because of carcinoma.

The Kahn reaction was negative.

Histologic examination of tissue from the leg showed a flattened epidermis, mantles of perivascular round cell infiltrate about the subpapillary blood vessels and many granules of hemosiderin in the upper part of the corium.

DISCUSSION

DR. S. W. BECKER: Clinically, there are a few cayenne pepper spots though little of the burnt sienna appearance in Schamberg's disease. Microscopically, the dermis was clear, with only a small amount of pigmentation in the papillary layers. I do not believe a definite diagnosis of Schamberg's disease can be made. I should be more inclined to favor some form of purpura.

DR. M. H. EBERT: I agree with Dr. Becker that neither clinically nor microscopically is this Schamberg's disease. The second diagnosis suggested a hypostatic eruption. That would fit the lesions on the leg, but a good many of these lesions were above the knee. It is certainly not Majocchi's disease. All that remains is some form of toxic purpura. What the cause is I do not know.

DR. MAURICE DORNE: When we first saw the patient it was our impression that she probably had Schamberg's disease. Since the original examination more of these lesions have developed; they varied somewhat but not sufficiently to change the clinical picture. After examining the biopsy section we could not make up our minds. I believe the patient has some form of purpura. She has no telangiectasia. Whether hypostatic purpura is the proper term for the eruption she presents, I do not know.

DR. M. H. EBERT: Have you made a determination of vitamin C to see whether she had a low vitamin C content? Occasionally that is present, though the patient gives a history of having had normal intake of food.

Lupus Erythematosus in a Young Child. Presented by Dr. H. Rattner and Dr. Marcus Caro and (by invitation) Dr. I. M. Felsher.

C. Z., a girl aged 7 years, entered the Mandel Clinic (Michael Reese Hospital) on Sept. 15, 1942, presenting a serpiginous erythematous maculopapular eruption with some scaling on the flush areas of the face, the bridge of the nose and the left ear. The eruption was first noted in April 1942. Except for the history of measles at 3 years and chickenpox at 4, the general health of the girl was consistently good. While she was under our observation the lesion on the right side of the face subsided gradually, leaving only several faintly red scaling maculopapules, but the lesions on the left side of the face and ear remained as they were.

On physical examination no abnormalities were found. The serologic reactions of the blood were negative, and the urine was normal. The blood count showed 4,400,000 erythrocytes and 6,700 leukocytes, with 53 per cent polymorphonuclear neutrophils, 38 per cent lymphocytes, 6 per cent monocytes and 1 per cent plasma cells. The Mantoux test gave a reaction of 2 plus, and the roentgenogram of the chest suggested a possible "hilus adenitis."

A biopsy was not permitted.

DISCUSSION

Dr. Theodore Cornbleet: The minimal amount of atrophy is noteworthy, and apparently there was one lesion on the right cheek that produced no atrophy at all. Did the youth of the patient have any influence on these results?

Dr. Oliver S. Ormsby: I should like to answer a question asked by Dr. Cornbleet. I have seen a number of children with lupus erythematosus, and they may show little or no atrophy for some time. One child of 6 years with lupus erythematosus was shown here many years ago (Arch. Dermat. & Syph. **9**:658 [May] 1924). Some of the lesions healed without atrophy, but after some years atrophy appeared.

Dr. I. M. Felsher: We presented this case not because we thought that the disease was a rarity but because it is still not common. In a search of the literature I found that one of the best contributions was made by Dr. Cummer (Arch. Dermat. & Syph. **24**:999 [Dec.] 1931). He stated that the incidence of lupus erythematosus before the fifteenth year of life varied in different groups from 2.3 to 11 per cent. He also found that the ratio for children was 7 girls to 3 boys. The disease has occurred as early as the first year of life and in some cases as early as the third month. It occurs in a greater incidence in the period from 10 to 15 years of age, being seven times as frequent as in the first five year period of life. The course of the disease with regard to type of lesion and response or resistance to therapy is similar to that in an adult.

Pemphigus Erythematosus. Presented by Dr. Harry M. Hedge.

Mrs. A. T., a white woman of English descent aged 81 years, for the past three years has had an eruption which began with bullae in the mouth and soon displayed erythematous patches on the back with some vesicles and bullae. At first the lesions were accompanied with much itching, but later the itching subsided. On two occasions the lesions have entirely cleared up; at other times all but a few red spots and a few pigmented patches disappeared. A few of the lesions which had been scratched now show white scars. The lesions on the cheeks and forehead have come and gone several times, and at present there are about five annular lesions on the cheeks and forehead and frontal region of the scalp. During the past year there has been almost a constant repetition of outbreaks, one starting before another was all cleared away. These outbreaks consist of the appearance at first of red patches about the size of a quarter. These are followed by several blisters around the periphery of the red lesion, and they may cause a uniting of several lesions to make one large plaque. There was a second eruption of blisters in the mouth two years ago, but at present there are none.

Two blood counts showed 6,750 and 8,200 leukocytes respectively. No biopsy was made. The urine showed no albumin. She has attacks of gallbladder disease occasionally, during which time she exhibits some icterus. Her blood pressure is 132 systolic and 78 diastolic. The pulse is rapid, usually about 103 beats per minute.

There have been lesions on the extremities during several of the attacks. There is practically no atrophy at the sites of the lesions. The course of the disease has been chronic. The Nikolsky sign has been positive several times, but today there is no sign of reaction over a region irritated yesterday. The patient has a good appetite and is in good general health for one of her age. She is rather deaf.

DISCUSSION

Dr. Oliver S. Ormsby: My conception of pemphigus erythematosus is that it appears as a syndrome with three distinct types of lesions, lupus-erythematosus–like lesions on the face, bullae and seborrheic dermatitis–like patches on the trunk. Usually there are seborrheic-dermatitis-like lesions on the scalp. On the trunk there are typical bullous lesions of pemphigus.

In the present case, though the disease has been present for several years, I believe it is pemphigus vulgaris rather than pemphigus erythematosus.

DR. EDWARD A. OLIVER: I agree with Dr. Ormsby.

DR. F. E. SENEAR: I agree with Dr. Ormsby. I should like to ask Dr. Ormsby whether in any cases he has observed there has been as much bullous involvement as in this particular one. I remember that some of his earlier photographs showed bullae, but I have never seen such profuse formation of bullae except in a case in which they changed to become pemphigus vulgaris.

DR. OLIVER S. ORMSBY: I agree with Dr. Senear. This woman has many more bullae than are normally encountered in the disease under discussion.

DR. F. R. SCHMIDT: I agree with the opinions expressed. I think this is an ideal case in which to use an organic arsenic preparation by mouth.

DR. RUBEN NOMLAND, Iowa City: I agree with Dr. Schmidt that in treatment of these mild forms of pemphigus one seems to get as good results with solution of potassium arsenite and similar preparations of arsenic by mouth as with other arsenicals.

DR. MAURICE OPPENHEIM (by invitation): I agree with Dr. Ormsby and Dr. Senear that the disease is pemphigus. It is interesting that the disease started four years ago with a bullous eruption in the mouth as the primary lesion of pemphigus vulgaris. That too should prove that it is pemphigus vulgaris. I suggest that the patient be treated with acetarsone.

DR. H. M. HEDGE: Nine months ago, three years after the onset, this patient had a typical lupus-erythematosus–like eruption on the face with lesions on the bridge of the nose and two separate lesions, one on either cheek. She has never at any time in the course of the disease shown loss of appetite or any serious septic state, and she has been active all of the time. There are a great many bullous lesions on the back and on the body that have been present for two or three months. While a patient with pemphigus erythematosus practically never has lesions on the extremities, this woman has had a rather large number of lesions on the feet.

A Case for Diagnosis (Monilethrix or Trichorrhexis Nodosa?). Presented by DR. S. W. BECKER.

R. B., a boy aged 17 months, has never had a normal head of hair. As the hair grew out, it was rubbed off at points of friction. Two of his paternal grandmother's cousins had "dry hair," and her brother's son has hair similar to the patient's but thinner. He also has red, dry elevations about the individual hairs. The patient's mother and maternal grandmother did not have any hair until they were 2 years old, after which it grew normally.

The patient's hair is dry and breaks off easily on rubbing. It is short (½ inch [1 cm.]) on the back and sides of the scalp, probably from rubbing the scalp on the pillow; on the vertex it is longer (2 inches [5 cm.]). Microscopic examination shows brushlike structures on the broken ends. The hair itself is seen to have regularly placed constrictions, between which are fusiform areas.

Treatment is being carried out by means of vitamin A in doses of 25,000 U. S. P. unit capsules twice daily and 2 cc. twice daily of the natural factors in concentrated liver extract and in crude riboflavin concentrate (solvamin), each dose of which has been enriched with 2 mg. of pyridoxine, 12 mg. of thiamine hydrochloride, 40 mg. of nicotinic acid amide, 12 mg. of pantothenic acid, 12 mg. of inositol (which encourages growth of hair in rats) and 1 mg. of riboflavin.

Hair is presented for microscopic examination.

DISCUSSION

DR. THEODORE CORNBLEET: There were large, yellowish gray patches on the back of the neck. Dr. Becker has been administering vitamin A. Could this account for these lesions with color not unlike that seen in carotenemia?

DR. I. M. FELSHER (by invitation): Was the child ever put under the Wood light?

DR. S. W. BECKER: I hoped that we would be given a little assistance in therapy, because the father is extremely eager to do something for the boy. The father states that his cousin has had an identical condition, progressive loss of hair as a child and not much hair as he grew up. When I first examined the hairs a couple of weeks ago, there were many more with fusiform swellings. The ones I extracted today, which were under the microscope, showed few swellings but showed brushlike ends where they were broken off. I do not have a great deal of faith in vitamin therapy, but I think it deserves a trial. I have not seen the lesions on the back of the neck. The scalp was not examined with the fluorescent light.

A Case for Diagnosis (Lupus Erythematosus?). Presented by DR. F. E. SENEAR and DR. M. R. CARO.

C. P., a white woman aged 52, first observed a red macular eruption on the side of the jaw about one year ago. As the redness subsided, there remained a residual pigmentation.

Since the onset there have been several exacerbations of redness, each being followed by an increasing area of pigmentation. During the past three months there has been occasional itching in the affected area and the patient has complained of a burning sensation in the mouth. She has lost about 45 pounds (20.4 Kg.) as a result of dieting; she has been eating no fish and little meat.

The eruption is limited to the face, neck and upper part of the chest, being fairly well demarcated by a lower border. There is a brown color throughout the affected area that is produced by a mixture of brownish pigmentation, telangiectases and a diffuse erythema. About the mouth and on the sides of the jaw there is a slight scaling. There is a slight but definite atrophy, especially on the sides of the neck.

Physical examination showed no abnormal conditions aside from those observed in the skin. The blood pressure was 122 systolic and 74 diastolic. Urinalysis gave results within normal limits. Examination of the blood showed: hemoglobin content, 85 per cent; erythrocytes, 4,500,000 and leukocytes, 6,000, with a differential count of 43 per cent lymphocytes, 5 per cent mononuclear leukocytes, 47 per cent neutrophils and 5 per cent eosinophils. The Kahn reaction of the blood was negative.

Histologic examination of tissue from the side of the neck showed atrophy and flattening of the epidermis, with intracellular edema, especially in the basal layer. The follicles were dilated. The upper part of the corium was edematous, and it contained many dilated blood vessels. About the blood vessels and especially about the follicles there were densely packed masses of lymphocytes and connective tissue cells. Just beneath the epidermis there were many large brown chromatophores. No iron pigment was shown when sections were stained. The elastic fibers were absent or fragmented just beneath the epidermis and about the hair follicles.

DISCUSSION

Dr. Oliver S. Ormsby: The chief point of interest in this patient from my standpoint is that with Drs. Ebert, Finnerud and my other associates I saw a patient some years ago whose case closely resembles the one under discussion. The picture was much like that of the poikiloderma of Civatte, but the disease later proved to be lupus erythematosus. This diagnosis should be considered here.

Civatte's poikiloderma and Riehl's melanosis have been considered identical, and the former disease is now being classed with the pigmentations. (See discussion on poikiloderma by Civatte, *Bull. Soc. franç. de dermat. et syph.* [*Réunion, Strassbourg*] **7**:848, 1929.)

Dr. C. W. Finnerud: I recall the case to which Dr. Ormsby refers. Within five years Dr. Coomber and I have seen a patient with an identical eruption, a school teacher 40 to 45 years old. The histologic section was practically identical with the one presented today. It suggested lupus erythematosus. With gold therapy and with bismuth therapy she made no progress. We convinced ourselves that cosmetics had nothing to do with the pigmentation in her case. We felt that we could rule out lichen planus, which has been considered in some of these cases. She returned in a year and was better. She came back six months to a year later for observation, and she had still a peculiar color. We saw her less than six months ago, at which time the eruption had disappeared and had left no trace. Apparently it cleared spontaneously. The histologic features were much as they are in this case. There was a decided atrophy of the epidermis, with hyperkeratosis, keratotic plugging of the mouths of the follicles and a vacuolation of the cells in the basal layer. I think also that the chronic lupus erythematosus character of the infiltrate in this patient was compatible with that diagnosis. I should be inclined to consider the disease an atypical form of lupus erythematosus.

Dr. M. H. Ebert: I have nothing to add except to state that the case which Dr. Ormsby mentioned made a tremendous impression on me. The present patient is the first I have seen since then with a disease nearly like the other. In the former case the termination was fatal. Acute lupus erythematosus disseminatus developed and the patient died.

Dr. J. H. Mitchell: I had this patient as one of the group for examination by candidates for certification by the American Board of Dermatology and Syphilology for an entire morning session. It was interesting that all the candidates named first poikiloderma of Civatte. I first saw this woman two and one-half weeks ago, and my impression is that the pigmentation is now much less than it was at that time. Also, the pigmented areas on the face are different from the lesions on the neck. Going into the history as best I could, because the patient speaks little English, I found that she had been using a cosmetic cream for a long time. The question is whether it contains ammoniated mercury. All dermatologists are familiar with the deposition of mercury from some of the mercurial creams.

Dr. Ruben Nomland, Iowa City: When Civatte described the poikiloderma which now bears his name, he described a clinical syndrome of pigmentation with atrophy and papular formation located chiefly on the face and neck and possibly on the arms. He thought that

the syndrome had not been previously described. Later he practically admitted that the disease he had described was essentially the same as the melanosis of Riehl. Irrespective of that, there is a syndrome of pigmentation of the face and neck and possibly of the arms such as he described. I think it should be pointed out that it is entirely different from the poikiloderma of Jacobi and from poikilodermatomyositis. It is a clinical syndrome of unknown cause, and lupus erythematosus and probably under certain circumstances poikilodermatomyositis may look a little bit like it. I agree that Civatte's original description was of a new syndrome which will probably differ from the melanosis of Riehl.

DR. MAURICE OPPENHEIM (by invitation): I remember that Rud. Müller reported a case of atrophoderma erythematodes reticulare with analogies to lupus erythematosus which was similar to this case; but I do not believe this patient has lupus erythematosus. There is a great similarity between the poikiloderma of Civatte and the poikiloderma atrophicans vasculare of Jacobi. The melanosis of Riehl and the melanodermatitis of Hoffmann and Habermann have a resemblance. I suggested that in many of these cases a pigmentation of the skin is due to local sensitization to light and to other external factors like tar, cosmetics and lubricants. I presented the case of a woman who contracted melanosis like Riehl's melanosis by cleaning cartridges with a lubricant. I believe the patient presented today has melanosis.

DR. S. W. BECKER: I questioned this woman carefully relative to her occupation and to the use of perfumes which might contain oil of bergamot. She said that she used a lotion with which I am not familiar. The grayish color of the skin makes, I think, the clinical diagnosis of postinflammatory melanosis. I first thought that the microscopic section was so typical for lupus erythematosus that that diagnosis would be my first choice.

DR. M. R. CARO: Many of the conditions observed in the histologic examination in this case are those encountered in lupus erythematosus; namely, atrophy of the epidermis, edema of the cells in the basal layer, plugging of the follicles and a cellular infiltrate about the follicles. The elastic fibers are absent in the upper part of the corium. There is no basophilic degeneration of the fibers beneath the epidermis, but aside from that the histologic picture is consistent with the diagnosis of lupus erythematosus.

DR. F. E. SENEAR: All the members of the American Board of Dermatology and Syphilology saw this patient, and they all had the same feeling that Dr. Mitchell expressed. We had considered the various diagnoses that have been proffered today with particular reference to pigmentation following the use of some cosmetic agents, lupus erythematosus, poikiloderma of Civatte and melanosis of Riehl. Incidentally, Dr. Ormsby has called attention several times to the fact that Civatte has accepted cases of his disease as melanosis of Riehl, but I assumed that not all the French dermatologists are in accord with them, because Petges, who wrote the section on poikiloderma in the "Nouvelle pratique dermatologique," gives a detailed differentiation between melanosis of Riehl and pigmentation of Civatte, listing twelve differential points. That leaves one in a quandary as to whether to accept the opinion of the man who first described poikiloderma of this type or to accept the explanation which Dr. Nomland offered today—and which I think is good—that there is a clinical picture which is not brought about by the factors which produce the melanosis of Riehl.

I think in view of the pathologic changes that a diagnosis of lupus erythematosus should be favored.

Rosacea-like Tuberculid of Lewandowsky. Presented by DR. E. A. OLIVER and DR. S. J. ZAKON.

Miss R. C., a white American woman aged 21, states that up to about three years ago she was in good health. She was treated for curvature of the spine by the use of body casts. About six months later she noticed scaling of the face and areas of redness. These persisted, and then she noticed the appearance of pinpoint-sized papules on the chin, cheeks and forehead. She consulted a number of dermatologists and received roentgen treatments, injections of a gold salt, about twenty-five injections of a bismuth compound, vitamins, irradiation with a water-cooled quartz mercury vapor arc lamp and generalized ultraviolet irradiation. A biopsy was performed about one year ago. The reaction to tuberculin was doubtful. She states that in spite of the aforementioned treatments there has been but slight improvement. She now shows a reddish eruption involving both cheeks, the chin and the center of the forehead. This eruption consists of a diffuse erythema and numerous discrete pinpoint or larger papules. On diascopic pressure they present an apple jelly color.

DISCUSSION

DR. L. M. WIEDER, Milwaukee: This patient has been treated several times recently by Dr. H. R. Foerster, through whose courtesy I had the opportunity to see her. I regret that I do not know more details of her past treatment, but I believe that she was treated extensively

with heavy metals before coming to us and has had some bismuth therapy recently. I am informed by Drs. Oliver and Zakon that they are presenting her today preliminary to giving her a new form of modified tuberculin therapy. One feature of her case that impresses me today is the variation in the rosacea exhibited; although it is common to encounter wide variations over short periods in the rosacea of patients with Lewandowsky's tuberculid, it is unusually variable in this patient. On one or two occasions she has shown congestive erythema which from a few feet away simulated an intense ultraviolet erythematous reaction, but today I hardly recognized the patient because of the pallor of the lesions. The tuberculous infiltrates themselves also seem less pronounced than usual.

DR. G. A. COOPER, Madison, Wis. (by invitation): I saw this patient three years ago, when the eruption first began on the face. There was a mild papular erythematous eruption with little scaling which responded to a sulfur lotion that I gave her. After that the eruption was apparently quiet for six or eight months. This is the first time I have seen her since. The picture today is nothing like that at the time I saw her.

DR. S. J. ZAKON: This girl, a medical student, heard about the inhalation of the fumes of tuberculin, and she came here to find out whether this form of therapy would be of value to her, since the standard therapy failed. I should like to ask Dr. Cornbleet whether he has had experience with this form of therapy in the treatment of tuberculids.

DR. THEODORE CORNBLEET: My colleagues and I have treated 2 patients with tuberculids by administering fumes of BCG vaccine. It seemed to me that in both cases there was definite improvement. In both of these patients there was a positive reaction to a 1:100,000 dilution of old tuberculin. I have observed that patients who respond to this type of therapy generally are sensitive to tuberculin. It is still too early, however, to make a definite statement about this. In the treatment of sarcoid this form of therapy has been of no benefit. In the patient under discussion the tuberculin test with a dilution of 1:100,000 produced a negative reaction. I wonder what the results of the test would be with stronger concentrations. On the basis of past performances, my guess would be, and it is only a guess, that the response to BCG therapy would not be as rapid or as good in this subject as in persons who are more sensitive to tuberculin.

Erythema Induratum (?). Presented by DR. J. H. MITCHELL and (by invitation) DR. F. W. HETREED.

M. B., a white woman aged 55, first noticed multiple swelling on the right calf two months ago. The onset was sudden. The swellings remained and were both painful and tender. In the past year she has had multiple roentgen treatments for enlarged glands in both axillas. Two years ago she had what apparently was erythema nodosum.

Examination shows multiple deep-seated pea-sized to cherry-sized nodules on the right calf. The nodules are attached to the overlying erythematous skin. There is no adenopathy at this time. A lipoma is present on the left anterior part of the wall of the chest.

The Kahn and Wassermann reactions were negative. Examination of the blood showed 4,100,00 erythrocytes and 5,550 leukocytes, with a normal differential ratio. The Mantoux test with a dilution of 1 to 100,000 was negative.

DISCUSSION

DR. EDWARD A. OLIVER: This was a most interesting case but one in which I am unable to make a positive diagnosis. The lesions felt and looked like erythema induratum.

DR. J. H. MITCHELL: The interesting thing about this case is that if the disease is erythema induratum it seems to have no favorite site. The patient had had a previous attack in the other leg. The rapid involution is striking. When I saw her last week, the lesions were much more tender than now, but they are rapidly undergoing involution.

Lichen Planus with Atrophy (?). Presented by DR. H. RATTNER and DR. M. DORNE.

Mrs. E. M., a Negro woman aged 42, presents an eruption on her legs of eight years' duration. It consists of variously sized and shaped hyperpigmented patches that contain hypertrophic papules, lichenified areas, scaly papules and tiny depigmented areas of macular atrophy, some of which have angular margins. The lesions involve the anterior and lateral surfaces of both legs. The eruption has been present continuously for eight years, and except for a tiny papule on the extensor surface of the left forearm other areas of the body have never been involved. There are no lesions in the mouth.

The Kahn reaction of the blood was negative.

Histologic examination of tissue from the leg showed changes consistent with the diagnosis of lichen planus.

DISCUSSION

DR. H. M. HEDGE: Some twelve or fourteen years ago Dr. Stillians and I had a patient with a similar eruption except that it was located on the shins and on the ulnar aspect of both forearms. It was diagnosed at the time as lichen planus with atrophy.

DR. HERBERT RATTNER: We presented the case only because it is rare to encounter lichen planus followed by atrophy. The interesting feature was the few lesions of macular atrophy, some of which had sharp borders. The histologic picture of some of the macular lesions is indefinite.

A Case for Diagnosis (Lymphoblastoma?). Presented by DR. F. E. SENEAR.

This patient was seen for the first time at the University of Illinois College of Medicine on April 28, 1942. He stated then that he had had a number of cutaneous lesions on his right cheek for the past six years and that during the past year the left cheek had also become involved. He had been treated for four or five years with old tuberculin, with little or no improvement in the lesions. Tests of the sputum and roentgenograms of the chest had been made and revealed no evidence of tuberculosis.

At the time of the first examination at the University of Illinois there was a nodular eruption of the center of both cheeks. The nodules were bluish red to yellowish red and appeared translucent on slight pressure. The nodules on the left side were hard, while those on the right side were softer. There was decided telangiectasia overlying the nodules. The nodules varied in size from that of a pea to that of a large cherry.

A definite clinical diagnosis was not made when the patient was presented at a meeting of the Chicago Dermatological Society, but a biopsy revealed chronic granulation tissue and dense fibrosis.

The patient was treated with roentgen rays, and the nodules all melted away by the time six treatments of 75 r each had been given.

On September 22 the patient returned complaining of pain and burning in the palate and left side of the jaw and under the left eye and ear. Examination of the palate revealed swelling and hyperemia especially on the left side, with hyperemia of the left upper alveolar process. A biopsy of the lesion of the palate showed edema of the epidermis and upper part of the corium, but otherwise these layers were within normal limits. In the lower part of the corium and extending deeply was a densely packed cellular mass which was sharply circumscribed above. This area contained many immature lymphocytic cells, varying greatly in size and staining properties, with scattered mitotic figures. In places there were elongated cells arranged in parallel whorls. The histologic picture suggested a malignant process.

DISCUSSION

DR. S. W. BECKER: There was one lesion on the anterior portion of the upper gum bed, rather translucent and telangiectatic, somewhat similar to what is encountered in some cutaneous epitheliomas. The microscopic sections contained an enormous number of round cells, most of which were flattened as a result of pressure. My guess would be that this is some sort of malignant tumor belonging in the group of white blood cell dyscrasias or among the sarcomas.

LIEUTENANT EUGENE A. HAND (MC), U. S. N. R. (by invitation): It was my impression that the lesions are malignant neoplasms, probably of the lymphoblastoma group.

DR. M. H. EBERT: I agree with Dr. Becker. Of course I have had the benefit of hearing Dr. Senear discuss this case informally. As I recall, the individual nodules on the cheek which were observed at the last presentation were of long duration and had not responded to therapy. A few exposures to 75 r of roentgen rays have cleared them up rapidly. That in itself would suggest new growths belonging to the lymphoblastoma group. The infiltrate in the section presented is not inflammatory but is of new growth type. The section was not clear enough to make out the type of cell. The lesion may be a lymphosarcoma or a lymphoblastoma.

DR. E. M. SMITH JR.: Of how long standing was the tumor in the palate?

DR. M. R. CARO: The first notation on the record about the lesion on the palate was dated Sept. 22, 1942. The lesions on the cheek were present for about six years prior to their treatment with roentgen radiation.

DR. E. M. SMITH JR.: I was wondering about a chronic granuloma, such as granuloma fissuratum or granuloma pyogenicum. However, in this case the involvement is rather extensive for such a consideration.

DR. F. E. SENEAR: I might refresh your minds somewhat by saying that this is the patient who had the persistent symmetrically placed nodular lesions on the cheeks. He was seen originally at the Central Free Dispensary, and biopsies at that time suggested a diagnosis of sarcoid. He was treated with tuberculin for a year or so without any result. The biopsies which have been performed at the medical school were not at all conclusive, and merely as a therapeutic experiment my colleagues and I wanted to see if we could cause any involution with roentgen rays. As Dr. Ebert said, after one of the early soft lesions had been treated it involuted 75 per cent in a week or ten days, and after that we went ahead and treated the denser lesions, which had been present for several years. They cleared rapidly. We felt that the rapid involution with radiotherapy indicated that the lesions were probably of the lymphoblastomatous type. The patient may have had the lesion on the palate for a long time, but he was not aware of its presence until last September.

A Case for Diagnosis (Gangrene?). Presented by DR. M. H. EBERT.

G. H., a man aged 76, states that prior to Dec. 3, 1942 no cutaneous complaints existed. On this date eruption similar to that present now occurred, accompanied by a pruritic and burning sensation. He states that he did not scratch or apply any medication at that time and has not done so since. A keratotic brownish coin-sized patch on the left side of the forehead, present when I first saw him (Dec. 7, 1942), has since disappeared.

An area of skin the size of a palm is hard, brown and leathery and is being sloughed off from the nucha by a gangrenous process. The helix of the right ear is similarly affected.

Physical examination revealed the following significant conditions: bronchial asthma and absence of pharyngeal and diminished corneal reflexes. Sensation was apparently normal.

Examination of the blood showed: hemoglobin content, 85 per cent; erythrocytes, 4,200,000, and leukocytes, 8,800, with a differential count of polymorphonuclear leukocytes 56 per cent, lymphocytes 26 per cent, monocytes 4 per cent, basophils 3 per cent and eosinophils 2 per cent. The Kahn reaction was negative. The urine was essentially normal.

DISCUSSION

DR. J. H. MITCHELL: I wonder whether there was a phenol burn. There was one streak across the right side of the head. The patient says he has not applied any medication. He admits drinking a little bit. I wonder whether he may not have dropped asleep against a radiator. The lesion appears to be an artefact, intentional or accidental.

DR. L. F. WEBER: He may have an artificial lesion; perhaps some one else threw phenol on his scalp.

DR. C. W. FINNERUD: I have seen lesions of this type occurring with gangrenous pyoderma. In a patient at the Cook County Hospital years ago who had severe hemolytic streptococcic endocarditis not only was the appearance of the lesion similar but we could determine that it was so deep-seated as to destroy by infarction all of the underlying tissues, inclusive of muscle. In another instance of severe pyoderma with hypertension there were multiple lesions of this character. It looks to me like a gangrenous process which probably is not self inflicted. The large lesion looks as if it might be the result of infarction.

DR. RUBEN NOMLAND, Iowa City: I think this is a superficial infection of relatively simple type in an original disease which could easily have been herpes zoster.

DR. L. M. WIEDER, Milwaukee: I wish to point out that the posterior margin of the right helix was involved, as though an external causative agent which produced the occipital injury had also made contact with the adjacent portion of the involved ear. I think this arrangement of the lesions is against infarction as an etiologic agent; also, if the history as obtained from the patient is correct, the sudden appearance of the lesions without appreciable subsequent spread is against an infectious causation. I believe they are artificially produced but not necessarily intentionally.

DR. J. H. MITCHELL: It is relatively easy to determine the presence of phenol in such black crusts by use of ferric chloride test solution. In medicolegal practice the phenol is distilled from the crusts.

DR. MAURICE OPPENHEIMER (by invitation): I think, as do Dr. Finnerud and Dr. Nomland, who suggest an acute infection, that this is an instance of gangrenous erysipelas. The man is 76 years old, and it is known that in a person of such old age erysipelas is gangrenous when it involves the scrotum and sometimes when it involves the face. Fever in such cases is always rare or absent.

DR. M. H. EBERT: We have been puzzled about the cause of the gangrene in this man. The transverse depression on the nucha looked as though it might have been caused by pres-

sure from a hot iron pipe. When it was first seen, the skin on the nucha was tanned like shoe leather and there was little inflammatory reaction. Today the dead tissue is separating. The necrotic lesion on the ear might suggest zoster, but the lesions were bilateral. There was no evidence of vesicles or pustules. We believed that the lesion was factitious but have been unable to cause the man to change his story. I am much obliged to Dr. Mitchell for his suggestion that the skin be tested for phenol. Gangrene from vascular obstruction can be ruled out. I believe this condition is self produced.

DR. RUBEN NOMLAND, Iowa City: I should like to call attention to something that Dr. O'Leary (O'Leary, P. A.: Sodium Amytal as Aid to Psychotherapy in Case of Dermatitis Factitia, ARCH. DERMAT. & SYPH. **36**:544 [Sept.] 1937) pointed out many years ago at a meeting of this society, that people with self-inflicted lesions can be induced to confess. If they are given a sufficient quantity of one of the soluble barbiturates (sodium amytal, for instance) they reach a stage where they will be willing to confess.

DR. M. H. EBERT: Is there not a possibility of getting a confession of something that had not happened or of an imaginary occurrence?

DR. RUBEN NOMLAND, Iowa City: I do not believe so.

Amyloidosis of the Skin. Presented by DR. E. A. OLIVER and (by invitation) DR. S. M. BLUEFARB.

R. J., a white man aged 61, a painter, states that he has had dermatitis on his legs for the past year. About ten years ago he had a generalized dermatitis, and at that time a diagnosis of lead poisoning was made.

Physical examination at present reveals hypertension (blood pressure of 160 systolic and 100 diastolic), severe gingivitis and pyorrhea with dental caries. There is no lead line. On his lower extremities extending from the knee to the ankle there are numerous excoriations, pigmentation and hypertrophic verrucous nodules. Injection subcutaneously of 1 per cent aqueous solution of congo red produced a positive reaction for amyloid. A frozen section stained with crystal violet showed the presence of amyloid. Urinalysis on Sept. 3, 1942 yielded essentially normal results except for a 1 plus reaction for albumin, and the blood count showed a hemoglobin content of 14.8 Gm., erythrocytes 4,530,000 and leukocytes 10,350, with a differential count of lymphocytes 30 per cent, polymorphonuclears 63 per cent, eosinophils 4 per cent, monocytes 2 per cent and basophils 1 per cent.

DISCUSSION

DR. RUBEN NOMLAND, Iowa City: In consideration of localized amyloidosis of the legs there are two other diseases to be considered. These are hypertrophic lichen simplex chronicus and hypertrophic lichen planus in which no other lesions are present, and perhaps one should consider hypertrophic dermatitis, in which lichenification is a great factor. These three cannot be differentiated with certainty by objective examination. However, localized amyloidosis is seldom verrucous as are the lesions in the case presented today. Second, if it is severe, the evidence of amyloid infiltration is definite in sections stained with hematoxylin and eosin. Masses of amyloid definitely circumscribed are found beneath the epidermis. In my opinion in the case presented the disease is either hypertrophic lichen simplex or possibly hypertrophic lichen planus. As nearly as I can tell, there was no evidence of amyloid in the section such as one would expect in amyloidosis of the degree as clinically presented.

A Case for Diagnosis (Lupus Erythematosus? Erythema Perstans? Erythema Elevatum Diutinum?). Presented by DR. M. OPPENHEIM and DR. D. COHEN.

J. W., a white man aged 47, presents an eruption on the face and ears. This is mainly on the left side and consists of sharply limited round-contoured papules ranging in size up to that of a nickel. Some of these papules are bluish white and surrounded by a red rim; others are intensely red, and a few have a central depression. There are no scales on the surfaces of these lesions, but enlargements of openings of the sebaceous glands are visible. There is a sensation of infiltration. The ears are red and somewhat edematous and covered by fine scaling. There is a superficial area of leukoplakia on the left buccal mucosa (the patient chews tobacco).

This eruption began five years ago in the month of January. It lasted until April and then disappeared. The patient has had recurrences every fall and winter and remissions every spring. The present attack began in November.

The urine and blood were normal; the Kahn reaction was negative.

DISCUSSION

DR. E. A. OLIVER: I have seen patients with erythema perstans whose lesions closely resembled those of this patient. I looked for signs of focal infection in the mouth but could find none.

DR. M. H. EBERT: I thought of a chilblain lupus. There are two types of chilblain lupus, lupus pernio, belonging to the sarcoid group, and Hutchinson's lupus erythematosus on a chilblain circulation. That was suggested by the recurrence in winter of a bluish discoloration of the face and ears. However, this man does not have a chilblain circulation. His hands are always warm, and he works outdoors. He said the color was due to some medicine that was given him, but it did not look as though it were the result of medication applied. I believe this is a case of lupus erythematosus.

DR. MAURICE OPPENHEIM (by invitation): I agree with Dr. Oliver, Dr. Ebert and Dr. Reuter. We wanted to show the patient from the standpoint of a differential diagnosis among lupus erythematosus, erythema facies perstans (Kreibich) and erythema elevatum diutinum, which was described by Crocker and Williams. We are really not able to make a diagnosis, though these four diseases come into consideration. Erysipelas perstans of Kaposi may be considered, too. There was no itching in the beginning. I do not think the eruption is due to cold. Erythema elevatum diutinum and erythema perstans are possibilities. Histologic examination will prove if one of these is right. The patient came under our observation yesterday.

DR. M. J. REUTER, Milwaukee: The patient had an infiltrated plaque on the right cheek, and there were a few papules on the left cheek. This plaque on the right cheek over the malar bone suggests the possibility of sarcoid.

A Case for Diagnosis. Presented by DR. E. M. SMITH JR.

A white boy aged 14 has an eruption which he states started in March 1942. The first lesion is still present on the back of his neck and consists of a dry squamous patch. In April other lesions appeared on the arms and back. Since then lesions have appeared on the lower extremities. The chest and abdomen have remained almost free of eruption. There is a disturbance of pigmentation at the sites of former lesions which resembles an incomplete vitiligo; exposure to sun did not produce pigmentation in these areas but did in the areas of normal skin. The patient's mother states that moderate changes in temperatures cause the lesions to become red and to swell for two or three hours.

The boy had an operation two years ago for removal of a gangrenous appendix.

No pathogens were found in the cultures.

DISCUSSION

DR. C. W. FINNERUD: I did not see the sections. The only diagnosis I could make was possible parapsoriasis. Some of the lesions had disappeared. I have seen lesions of parapsoriasis disappear and leave similar depigmentation.

DR. F. E. SENEAR: I felt very much as Dr. Finnerud did. There was one thing that was rather striking, the symmetrically distributed lesions in the posterior axillary fold, which were circumscribed and crescentic. It should be kept in mind that in many cases what early seems to be parapsoriasis later is found to be mycosis fungoides. The configuration in the present case is the only reason for thinking of mycosis fungoides.

DR. M. H. EBERT: There was one thing that was somewhat confusing to me in the history. It was stated that the first lesion that ever appeared was still present, which implies that all the lesions are still present. The area of partial depigmentation which, as Dr. Ormsby pointed out, is not a true vitiligo, would indicate that he had an extensive eruption on the back. I should like to ask Dr. Smith if there was such an extensive eruption. I am inclined to believe that the disease is parapsoriasis.

DR. RUBEN NOMLAND, Iowa City: Dermatologists encounter a great deal of dry dermatitis in patches that leave behind them depigmentation. I do not think that they are parapsoriasis; neither do I think that they are infectious dermatitis, and I do not by any stretch of the imagination think that they are the premycotic stage of mycosis fungoides. They are observed in persons who consult a dermatologist because they have been to a physician for some other disease and he was concerned about these areas. These dry scaling areas are common; I do not know what they are. I cannot fit them into the diagnosis that was given today or into any that I know of.

DR. G. A. COOPER, Madison, Wis. (by invitation): I am apparently in Dr. Nomland's territory because I have seen one boy with lesions strikingly like these. The original complaint was that he had depigmented areas which did not tan in the summertime. He had lesions like those on the left shoulder of this boy. There was an increase in keratotic follicular involvement. That boy was tested by an allergist, who found him sensitive to wheat. When wheat was eliminated from his diet, the process cleared in the summer. Toward the latter part of the summer the eruption recurred when he ate wheat once more. Removal of wheat from the diet caused the eruption to clear.

DR. E. M. SMITH JR.: I am sorry not to have more material, but I have seen the patient only twice. According to the history he had no eruption on the chest, but he now has cutaneous changes which look like relics of lesions. The history also stated that the lesions cleared once during the period. Incidentally, he has been given a 20 per cent thiosulfate lotion, and he has made definite improvement. In the absence of cultures positive for some pathogen, I do not know how to diagnose the disease.

A Case for Diagnosis. Presented by DR. M. DORNE.

F. T., a white man aged 41, presents an eruption of twenty years' duration. The patient states that at the onset there was a widespread intensely pruritic eruption of small vesicles. The face was never involved. He was treated for the first five years with roentgen and ultraviolet radiation and various local medications. He has had no treatment during the past fifteen years. At the present time there is hyperpigmentation involving the legs and thighs and extending upward to end sharply on the midportion of the trunk. On the legs there are various-sized and variously thickened papules and nodules, atrophic areas and scars. A similar but less extensive eruption is present on the forearms and arms. There is bilateral inguinal adenopathy.

The Kahn reaction was negative. An examination of the peripheral blood showed normal numbers of cells and a normal hemoglobin content. The differential count was 66 per cent neutrophils, 6 per cent eosinophils, 16 per cent lymphocytes and 12 per cent monocytes. The blood platelets were normal.

Histologic examination of a biopsy specimen from the leg showed a slight and irregular acanthosis and a thin scale with islands of parakeratosis. Throughout the corium the walls of the blood vessels were thickened, some to the point of occlusion of the lumen, and about each group of vessels there was a circumscribed, loosely packed round cell infiltrate. The intervening connective tissue fibers were thickened and densely packed.

DISCUSSION

DR. MAURICE OPPENHEIM (by invitation): If I should venture to make a diagnosis in this case I should say lichenification. The square projections of the epidermis in the cutis, in which edema, round cell infiltration and induration of the connective tissue are the histologic changes, are characteristic of lichenification. The extensor sides of his legs are more involved than the flexor sides; hence I thought of some kind of prurigo in an adult (the patient is 41 years old). Little nodules break out which are hard and yellowish red and more easily felt than seen. It is striking that in this case the location is unilateral in the lumbar area. The left side is absolutely free. That does not fit into the diagnosis of prurigo; hence the man may have lichen chronicus simplex.

DR. M. R. CARO: This is an interesting case because of the strikingly linear border limiting the upper part of the eruption. I have nothing to offer in the way of a diagnosis clinically or histologically. An outstanding feature in the section is the enlargement of and the cellular infiltration about the nerves in the corium. I have observed that type of inflammation in cases of prurigo nodularis, although there is nothing else in this case to suggest that diagnosis.

DR. MAURICE DORNE: I was hoping there would be more discussion of this case. I have not been able to make a diagnosis. Some features vaguely suggest the possibility of dermatitis herpetiformis, and some features suggest prurigo nodularis. However, the histologic sections from a lesion on a leg and from an inguinal gland are not compatible with these diseases.

Lupus Erythematosus of the Eyelid. Presented by DR. H. RATTNER and DR. M. DORNE.

W. C., a Negro aged 38, presents an atrophic patch on the middle third of the margin of the right lower eyelid. Behind the left ear there is a circinate patch about the size of a dime which has a narrow erythematous zone, atrophy in the central portion and some scaling and in the lower border an erosion the size of a split pea. The left postauricular lymph

node is enlarged. Patches of depigmentation without atrophy are present on the glans penis and on the prepuce. All of the lesions have been present for the past fourteen months.

The Kahn reaction was negative.

Histologic examination of a section from the lesion behind the left ear showed atrophy of the epidermis, with edema of the basal layer and horny plugging of the dilated follicles. In the upper part of the corium there was a densely packed lymphocytic infiltrate, and these cells extended more deeply as circumscribed mantles about the follicles and blood vessels.

DISCUSSION

DR. L. F. WEBER: I should not attempt to make a diagnosis of lupus erythematosus by looking at the section from the eyelid alone. I have always thought it is enough to have one disease; I should not diagnose two diseases for him.

DR. M. H. EBERT: I have seen lesions of lupus erythematosus of the mucous surface of the eyelid which were exactly like this, well defined and associated with lupus erythematosus in other parts of the body. I see no reason for denying the diagnosis. I think Dr. Finnerud was the first to call attention to the number of persons with lupus erythematosus who have lesions of the mucous membrane of the mouth. If lesions in the lower lid are looked for, they will be found more frequently.

DR. HERBERT RATTNER: The diagnosis was not made from the lesion on the eyelid alone. It was only after we had seen the lesion on the ear that we considered the diagnosis of lupus erythematosus for the eyelid lesion.

Lupus Vulgaris. Presented by DR. J. H. MITCHELL and (by invitation) DR. F. W. HETREED and DR. R. H. SCULL.

G. D., a white man aged 54, was presented at the April 1942 meeting. He is shown again to demonstrate the rapid growth of this particular type of lesion. The Kahn and Wassermann reactions were repeatedly negative. Antisyphilitic therapy administered two years ago brought about no change in the lesion. A Mantoux test with a 1 to 10,000 dilution of old tuberculin elicited a positive response.

Therapy consisted of injections of starch. The patient is at present receiving irradiation from a quartz mercury lamp, and some improvement has resulted. The color slide showed the lesions as they were a year ago.

Histologic examination of a nodule removed from the left cheek showed thinning of the epithelium, with little other change. The corium contained a large number of giant and round cell tubercles. With special staining Koch bacilli were demonstrable.

DISCUSSION

DR. L. F. WEBER: I was thinking of the possibility of a malignant growth in the lesion on the upper lip, particularly on the right side, extending to mucous membrane.

DR. C. W. FINNERUD: It would be interesting to have a biopsy of the soft lesion of the upper lip to determine whether it is tuberculosis verrucosa cutis or squamous cell epithelioma.

DR. HERBERT RATTNER: What has been the experience of the members with the treatment of lupus vulgaris with starch? In this case there has been an excellent result.

DR. OLIVER S. ORMSBY: I think that injections of starch work well for small areas, but much time is required to get results. In 1 of our patients treated by Dr. Ranquist a patch about the size of a silver dollar was removed in about eight months' treatment (Lupus Vulgaris Successfully Treated with Injections of Starch, ARCH. DERMAT. & SYPH. **42**:185 [July] 1940.

DR. THEODORE CORNBLEET: As a result of reports from St. Louis of improvements in patients with lupus vulgaris from the injection of a starch suspension, my colleagues and I selected a few subjects for a similar treatment. Our patients did not seem to obtain enough improvement to warrant the continuation of this form of therapy. We made injections into small marked-off areas as many as seven or eight times in as many weeks. Involution at these sites was questionable.

DR. J. H. MITCHELL: I thought the case was interesting in view of the rapid extension of the process and because the patient has been shown here before. The lesion on the lip may be a squamous cell epithelioma or an ordinary wart. The treatment the man is getting now is radiation from a quartz mercury vapor lamp, phosphated cod liver oil and a salt-free diet. I am not sure that he is adhering to instructions as to diet and medication.

Report of Cultures of Sporotrichosis. DR. J. H. MITCHELL.

Some of the members may have seen the cultures in the case of sporotrichosis shown at the last meeting. I was asked to see the patient in the hospital. The cultures made in the hospital were negative. I saw the patient on Friday following the meeting and made a series of cultures with Sabouraud's medium and all were positive. I have called attention in demonstrations to the technic of planting the pus on the surface of the culture tube. This was suggested by Gougerot, who pointed out that within forty-eight hours the microscopic examination will reveal the presence of myceliums. They can be shown easily with the low power (no. 15 eye piece). Which organism it is I have not as yet determined. The pronounced pigment would suggest Beurmann's rather than Schenck's.

UDO J. WILE, M.D., *President*

MICHAEL H. EBERT, M.D., *Secretary*

Jan. 20, 1943

Chronic Undermining and Burrowing Ulcer (Meleny). Presented by DR. M. H. EBERT and DR. M. OTSUKA (by invitation).

M. O., a Polish woman aged 55, states that in April 1942 she had a "boil" on the mid-pubic region which opened spontaneously, leaving a small ulcer. This has spread continuously for the past nine months in spite of the use of all sorts of local applications. Within the past month another "boil," which now is a fluctuant abscess running along the nasolabial fold, has developed on her right cheek. The patient is extremely weak and emaciated.

General physical examination reveals nothing significant except anemia.

The entire lower half of the abdomen is occupied by a shallow ulcer with granulating surface and irregular, undermined border which is erythematous. Cultures of material from active margins of the ulcer disclosed small colonies of nonhemolyzing streptococci which grew under partially anaerobic conditions. She has a mild albuminuria.

The Wassermann and Kahn reactions of the blood were negative. Examination of the blood showed a hemoglobin content of 54 per cent, 2,850,000 erythrocytes and 10,500 leukocytes, with a normal differential count.

She has had four blood transfusions of 500 cc. each in the past three weeks. She is taking sulfanilamide by mouth, and the blood level of the drug is 15 mg. per hundred cubic centimeters. At present she is using zinc peroxide medicinal and awaiting surgical débridement.

DISCUSSION

DR. LOUIS A. BRUNSTING, Rochester, Minn.: This patient presents a large, destructive ulcerative process of the abdominal wall, the characteristic feature of which lies in the advancing margin, where there is moist gangrene, bluish discoloration and a progressive necrosis of the tissues. I believe this is pyoderma gangraenosum in association with chronic ulcerative colitis. The organisms that are usually found are nonhemolytic streptococci and forms of staphylococci. In the condition described by Meleny there may be the same rapid peripheral extension of the process, but usually there is more subcutaneous burrowing and cultures reveal microaerophilic hemolytic streptococci.

In such cases there may or may not be a disturbance of the general health, and treatment of the lesion is by thorough débridement and implantation of zinc peroxide or some other antiseptic, such as a sulfonamide compound, locally and systemically. In pyoderma gangraenosum the local treatment of the lesion is of secondary consideration; the main problem is the control of the systemic disease, and to this end multiple blood transfusions, rest in bed, sunlight and systemic use of one of the milder sulfonamide compounds, such as azosulfamide or sulfaguanidine, are also helpful. The use of vaccines is not recommended, because the trauma to the skin may set up other foci of abscesses and ulcerations.

DR. UDO J. WILE, Ann Arbor, Mich.: It is interesting that Dr. Brunsting mentioned the association of the ulcer with colitis. Ulcers of this type are occasionally seen in association with amebic dysentery. The first case of this condition in the United States was reported by Dr. Martin Engman Sr. under the title of "Amebiasis of the Skin."

I have had such a case in which Endamoeba coli was isolated from the skin of a woman who had a large ulcer of the leg following severe amebic dysentery, from which she had recovered.

I should like to ask Dr. Brunsting whether any of the patients at the Mayo Clinic were found to have amebiasis.

DR. LOUIS A. BRUNSTING: Not one.

DR. J. H. MITCHELL: About twenty years ago I presented a patient here with an extensive burrowing and undermining ulcer on the left arm caused by hemolytic streptococci. Dr. Finnerud came to the office several times to see if he could see motility in epithelial cells which I thought might be amebas. The patient, a young man, had no intestinal trouble whatsoever. He finally made an uncomplicated recovery after being in Presbyterian Hospital, where I used dilute solution of sodium hypochlorite and, contrary to Dr. Brunsting's advice, vaccines. The patient was shown at a meeting of this society the proceedings of which were lost by the secretary (to my knowledge the only time such a thing happened).

DR. RICHARD S. WEISS, St. Louis: I think one can sometimes differentiate clinically the amebic type of ulcers from the type this patient presents. I had the good fortune to observe the cases Engman first presented, and there have been several cases presented since then. The character of the ulcer is somewhat different. Instead of a rolled border that gives the impression of either blastomycosis or an epitheliomatous change, the amebic type of ulcer has a border that is not particularly elevated. It is characterized by spreading centrifugally and is bordered by a 1 to 1½ inch (2.5 to 3.8 cm.) band of erythema, which generally has a definite bluish color. There is definitely undermining of this area. When there are ulcers of this type, one looks for amebas. They are usually easy to find on the warm stage under the microscope. The patients I have observed in later years—I have had none in recent years—got well from thorough cauterization well beyond the border of the bluish erythema.

DR. C. W. LAYMON, Minneapolis: I think Dr. Brunsting's observations concerning hidradenitis suppurativa and pyoderma are important. At the University of Minnesota a case of pyoderma gangraenosum was recently observed in which zinc peroxide and sulfathiazole therapy were used unsuccessfully. In this instance there was noteworthy benefit when penicillin was used, even though the patient eventually died. Penicillin is worthy of trial in some of these cases.

DR. THEODORE CORNBLEET: I think the nutritional aspects were well outlined by Dr. Brunsting. Patients with ulcerative colitis and with large cutaneous ulcers like these lose proteins. They need to be replenished. These patients seem to do better when amino acids are administered intravenously rather than by any other route. It may be that they do not absorb protein well when taken by mouth. Solutions of amino acids may be applied locally, too, on the skin. It could be interesting to watch what such a regimen would do for this patient.

DR. CLEVELAND J. WHITE: Dr. Brunsting spoke about the usual association of this type of lesion with colitis. His suggestion about general measures is pertinent, particularly as it comes from a surgical center. However, I have seen 3 patients in whom there was no ulcerative colitis associated with the cutaneous ulcer. The first 2 recovered with treatment by fulguration followed by administration of a sulfonamide compound. In the case of the third a cure was effected without any surgical measures, by use of sulfonamide compounds plus supportive therapeutic medical measures.

DR. UDO J. WILE: Incidentally, this patient has been taking sulfonamide compounds by mouth and has used local applications of zinc oxide ointment.

DR. M. H. EBERT: I should like to ask the men from the Mayo Clinic if they are familiar with Meleny's undermining and burrowing ulcer and know how it differs clinically from this type of ulcer. Perhaps Dr. Brunsting would like to discuss this.

DR. UDO J. WILE: A patient with an interesting example of the Meleny type of ulceration was brought to the University Hospital about two years ago. The destruction in this case was far more extensive than in the case shown here. The tendon sheaths and musculature were completely exposed. One foot sloughed off at the ankle joint, and the patient died within a month or two after his admission. This case was characterized by an extraordinary absence of pain. The patient was seen by all the surgeons, and careful studies were made from the standpoint of bacteriology as well as pathology. The consensus was that the ulcer belonged to the group described by Meleny. I do not believe that in the case under discussion the lesion is of this type.

DR. M. H. EBERT: I purposely used the term "chronic burrowing, undermining ulcer of Meleny" to stimulate discussion. Dr. Otsuka, resident at the Cook County Hospital, says that my original diagnosis was pyoderma gangraenosum. He was sufficiently interested to discuss this case with Dr. Cole, head of the department of surgery at the University of Illinois, who had become interested in this type of burrowing, undermining ulcer. The patient has had

four blood transfusions, a high protein diet and the local application of sulfanilamide, without response; so I thought there was a possibility that the ulcer might belong to the other group.

I have encountered two very excellent examples, one of which was a diffuse destructive ulcer. Both patients were in Dr. Ormsby's service at Presbyterian Hospital. The first case I have discussed many times at various meetings of this society. It was observed before Dr. Brunsting and his colleagues at the Mayo Clinic described these ulcers. The predisposing factor was severe anemia due to hemorrhages from the bowel. The man's life was saved by blood transfusions. He recovered and had no recurrence.

The second case from Dr. Ormsby's service was that of a middle-aged man who was in Presbyterian Hospital under Dr. Ormsby's and Dr. David's care for a long time with a destructive undermining ulcer of the leg. That ulcer was of the type Meleny described. Such an ulcer goes down to the fascial planes and undermines more thoroughly. Very often new satellite foci form and break down. It gives a different picture than that of this patient. However, Greenebaum, in the article that Dr. Brunsting mentioned, seemed to be of the opinion that these should be described as vegetating ulcers. I think there is a question of nomenclature. It should be emphasized that bacteriologic studies alone are not sufficient to identify the ulcer. Meleny expressed the opinion that in burrowing undermining ulcer of severe type the organism is always an aerogenous hemolytic streptococcus. The first choice of treatment is zinc peroxide. On the other hand, the type presented here today and the type Dr. Brunsting described, pyoderma gangraenosum, is described as caused by nonhemolytic streptococci in association with Staphylococcus aureus. I do not know whether the bacteriologic findings in all these cases would be identical. In this particular case the woman has not responded as well as she should. We had planned to try zinc peroxide treatment in perhaps a more efficient fashion than we had been doing. It has also been pointed out that the quality of zinc peroxide may vary from batch to batch, and tests should be made to determine whether an efficient preparation is being used.

I think this patient's disease probably should be termed pyoderma gangraenosum. I agree with Dr. Brunsting. I used the other title to see if I could get any discussion.

A Case for Diagnosis (Erythema Induratum?). Presented by DR. MICHAEL H. EBERT.

R. C., a 15 year old girl, was presented before the Chicago Dermatological Society in October 1942. The discussion at that time turned on the possibility of an unusual perivasculitis. Some time later the patient was given 15 drops of potassium iodide three times a day. In five days the infiltrated plaques broke down spontaneously, and they have shown little tendency to heal since then. Cod liver oil ointment and sulfathiazole have been used locally. There is no history of tuberculosis in the family or environment. The patient had rheumatic fever at the age of 6 years.

She now presents a punched-out deep ragged ulcer 4 cm. in diameter on each calf.

Examination of the blood showed a hemoglobin content of 67 per cent, 3,710,000 erythrocytes and 8,200 leukocytes, with a normal differential count. The blood chemistry was normal. The Wassermann and Kahn reactions were repeatedly negative. The Mantoux test with old tuberculin in dilutions of 1:1,000 to 1:100,000 elicited negative responses. The reaction to a Frei test was negative. Nothing significant was encountered in the roentgenograms of the lungs or of the bones of the legs.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: With every patient presented with an indurated plaque or plaques of the leg, the question of erythema induratum comes up. As is well known, the name in itself is not good, but usage has established it, and it will probably remain in the literature. The causation is always in doubt, and although in certain cases there are enough features to warrant ascribing it to tuberculosis, there are many in which tuberculosis is not tenable as a cause.

DR. C. W. FINNERUD: I think the most conclusive thing about the section presented, if it is deep enough, is that it is not characteristic of erythema induratum. Erythema induratum presents a rather definite microscopic picture, there usually being a tuberculoid reaction in the lower part of the cutis and hypoderm. I am not able to classify these ulcers, but I believe that the disease is not erythema induratum.

DR. PAUL A. O'LEARY, Rochester, Minn.: Until a year ago I thought of erythema induratum as a clearcut clinical entity, not difficult to diagnose, of tuberculous origin. However, since it has become the practice at the clinic with which I am associated to study by biopsy all nodular lesions on the lower extremities, especially on the posterior aspects of the leg, my clinical concept of this disease is by no means as clearcut as it was formerly. Many of

the recurring nodular and ulcerating lesions found on the posterior aspect of the lower third of the leg which have the characteristics of Bazin's disease do not show a tuberculoid structure but do demonstrate varying degrees of occlusive disease of the blood vessels.

The patient presented has a history of having had pneumonia some years ago which necessitated approximately three months of hospitalization, after which she has had edema of the ankles. This sort of a history is most significant to me, because I believe that edema per se, indicating some vascular abnormality in the extremity, is more significant in producing the disease than is a tuberculous infection, indicated by roentgen evidence of healed pulmonary tuberculosis or by a positive reaction to tuberculin. Neither do I believe that the edema need be great enough to produce obvious pitting, since microscopic edema in the leg may be just as significant. The belief that vascular disease, especially as it affects the veins, is a significant factor in the cause of erythema induratum has been strengthened by the results obtained from the use of Pará rubber bandages. An elastic bandage does not produce sufficient support for patients with this disease, while a 3 inch (7.5 cm.), 50 per cent Pará rubber bandage, worn from the toes to below the knee, not only heals the ulcers but prevents recurrence of the nodules as long as the bandage is worn. It is unfortunate that these bandages are next to impossible to get at this time.

This study is far from complete, but up to the present results indicate that disease of the blood vessels, probably of the venous vessels, is of paramount importance in causing Bazin's disease.

DR. UDO J. WILE, Ann Arbor, Mich.: I should like to ask Dr. O'Leary if he has found that the nontuberculous types of erythema induratum are also associated with the habitus characterized by stocky legs, which is so commonly observed in patients with the tuberculous type of erythema induratum.

DR. PAUL A. O'LEARY: It is also our experience that these lesions, as a rule, are found in the husky or stocky, piano-legged type of young woman.

DR. OLIVER S. ORMSBY: I should like to ask Dr. Ebert how long this patient had the lesions before they broke down and ulcerated. When the patient was previously presented, there was no ulceration.

DR. M. H. EBERT: These plaques on the sides and the ulcers were always very puzzling to me and to others. At one time I thought they were a variety of deep scleroderma, perhaps dermatomyositis of an unusual type. At one time my colleagues and I thought they represented an amyloid type of degeneration. They certainly did not resemble erythema induratum. They were slightly yellowish and extremely hard.

To answer Dr. Ormsby's question, these plaques were present for at least ten months before the area broke down. The area broke down on both sides simultaneously about five days after the administration of sodium iodide was begun. Whether that has any bearing on a possible tuberculous causation or whether it has to do with a vascular disease I do not know. Dr. Slepyan, in the laboratories of the University of Illinois, made a thorough study of the sections in a search for tuberculosis. That may be present clinically, but the results of all the studies were negative.

I am rather inclined to agree with Dr. O'Leary that it is a vasculitis of some cause other than tuberculosis. It is not erythema induratum, if by that is meant Bazin's disease, which is caused by tubercle bacilli.

DR. L. F. WEBER: I should like to ask Dr. O'Leary whether vascular damage was demonstrated by means of roentgen or by means of infra-red photography.

DR. PAUL A. O'LEARY: We have not used infra-red photography with any degree of regularity to demonstrate vascular disease in these patients. Temperature studies have not shown any appreciable change in the arterial vessels, and I am still of the belief that edema per se plays a more significant role than does involvement of the small vessels.

Arrested Acute Disseminated Lupus Erythematosus. Presented by DR. THEODORE CORNBLEET.

G. S., a white unmarried woman aged 36, became ill four years ago. At that time patches developed on her face. Soon afterward the eruption became generalized, with the development of fever and toxemia. When I first saw her, the eruption was that of a classic type of acute disseminated lupus erythematosus and she was profoundly ill. With treatment with parenterally administered liver extract there was decided improvement which continued for several months. There were relapses at intervals with fever. The worst relapse followed a period during which liver extract was not given. Fever again developed, the temperature ranging as high as 100 F. Intramuscular injections of 25 per cent solution of nikethamide (pyridine-

3-betacarboxylic acid diethylamide) were added. These seemed to improve her subjectively, and the temperature remained more nearly at a normal level, although it did rise slightly some days. It was found that there were foci of infection around some of the teeth. Four teeth were removed. A culture showed the presence of hemolytic streptococci. Residual pigmentation of the skin has slowly disappeared. The patient feels well and has no fever.

DR. UDO J. WILE, Ann Arbor, Mich.: There have been many cases of lupus erythematosus that terminated the other way.

DR. ARTHUR CURTIS, Ann Arbor, Mich. (by invitation): This case was interesting to me because improvement apparently began when the patient received injections of liver extract. It has been shown, at the University of Chicago, that paraaminobenzoic acid quantitatively absorbs ultraviolet rays. Crude liver extract is high in paraaminobenzoic acid, and it may be that the patient's improvement was due to the ability of this vitamin to absorb ultraviolet rays.

DR. FRANCIS E. SENEAR: There are two things in this situation worthy of mention. No one has commented on the use of nikethamide in this case. I think that in closing Dr. Cornbleet might give his ideas as to why he used it.

A patient whom I had in the hospital for some time and who died just last week presented a severe type of acute disseminated lupus erythematosus which improved materially with the use of injections of liver extract. At Dr. Cornbleet's suggestion the use of nikethamide was added to the treatment, and her improvement continued, possibly at a somewhat accelerated rate. My patient had a number of infected teeth, but she never improved to the point where it was felt that it was safe to interfere with these foci of infection, and I should like to ask for an expression of opinion with regard to the removal of foci of infection in such circumstances. Warning has always been given about the danger of interfering with such foci when the patient is acutely ill.

In the patient presented today, the infected teeth had been removed after she had been free of fever for but a short time, and apparently there were no ill results from this procedure. With the aforementioned patient, there were several periods of two to three days when she was free of fever but an elevation of temperature always followed immediately after these short intervals of normal temperature; consequently, I was reluctant to regard these short periods of freedom from fever as an indication that the teeth might be removed.

DR. RICHARD WEISS, St. Louis: I was intrigued by the use of nikethamide. I hope that Dr. Cornbleet will speak of it. I should like to ask what type of liver extract he used and whether or not it was the highly refined type that is useful for pernicious anemia.

DR. THEODORE CORNBLEET: The liver extract is a highly refined variety and is given subcutaneously. It produces much less reaction than the crude extract. If one uses crude liver extract, more of it has to be used and it is much more painful. The essential point, however, is that the refined material is ineffective. It contains no B vitamins.

DR. UDO J. WILE: Am I right in believing that the infectious attack followed discontinuance of administration of the liver extract?

DR. THEODORE CORNBLEET: Yes.

DR. M. H. EBERT: Dr. Cornbleet apparently does not agree with Dr. Paul Gross about the use of crude liver extract, feeling perhaps that he gives a greater variety of vitamins.

DR. UDO J. WILE: No mention was made of the presence or absence of nephritis during this patient's acute illness. Did this patient present any evidence of nephritis?

DR. THEODORE CORNBLEET: She showed no evidence of nephritis. This patient is one of several having the disseminated form of lupus erythematosus who have been under my observation and continue to show a satisfactory clinical response. Their treatment consists of use in daily alternation of a refined liver extract and nikethamide. Nikethamide has properties of nicotinic acid and besides is a stimulant. In an unpublished work I have found that in photosensitive persons with increased excretion of porphyrin nicotinic acid is capable of reducing this excretion and sensitivity. Liver extract may be useful as a substitution product, or increased requirements are present in the liver, where porphyrins are thought to be produced. This therapeutic regimen has caused an improvement in the clinical state in each of these groups of patients. In some there are complete remissions. These improvements and remissions, unfortunately, are but temporary. Nevertheless, they are of extraordinary importance, for I have found invariably present in each of these subjects septic teeth, which can safely be removed during these breathing spells. I do not imply that all patients with this disease will eventually be found to have sepsis of the teeth. It is well known that removal of septic teeth in the acute variety of disseminated erythematous lupus hastens death. If,

however, the patient is first prepared by liver and nikethamide or nicotinamide, nothing more serious happens than a small rise in temperature. It is my practice to extract one tooth weekly as soon as the patient feels and looks better, even though a temperature up to 100 F. is present. As many as three teeth at a time have been extracted from some patients when it could be risked without too serious immediate results. Valuable time must not be wasted in waiting to remove septic teeth; otherwise the usual fatal issue will result. Undue conservatism is to be deprecated in a desperate situation in which heroic action is called for. The therapeutic art here lies in the proper timing of dental extractions after proper preparation with substitutive agents. It seems that foci of infection—in this group of patients, found under the teeth—are capable of dissipating certain nutritive elements or that in the presence of these infections the body requires more of certain elements. A parallel situation holds for fever and vitamin C. While it is difficult to satisfy entirely the need for vitamin C during high fever, nevertheless, its administration can tide the patient over a situation.

Tetryl Dermatitis. Presented by DR. JAMES H. MITCHELL and (by invitation) DR. A. S. ROMBERGER.

A man aged 54 entered the Presbyterian Hospital on Jan. 6, 1943 with severe dermatitis of the entire forehead, face and neck. He had worked for nine days with tetryl before the dermatitis developed on the face and neck. He was laid off for one week, at the end of which time the dermatitis cleared, but it immediately recurred on his return to work.

On the day of his admission to the hospital there was a severe erythematous and scaling dermatitis involving the entire forehead, face and neck. The palms were stained deep orange. One-half skin unit of unfiltered roentgen rays (75 r) was given to the head and neck, and 10 per cent naftalan in zinc oxide paste was applied to the affected areas. Great improvement resulted, and the patient was discharged on January 12 with his skin practically cleared.

Tetryl Dermatitis. Presented by DR. JAMES H. MITCHELL and (by invitation) DR. A. S. ROMBERGER.

A man aged 51 entered the Presbyterian Hospital on Jan. 8, 1943. The dermatitis developed about December 20 on the forehead, face and neck and grew rapidly worse. The palms were stained deep orange. On arrival at the hospital the forehead, face and neck were given ½ skin unit of roentgen rays (75 r). There being no available bed, the patient was not admitted until the following day. Since then he has been treated with 10 per cent naftalan in zinc oxide paste. Erythema and itching persist.

DISCUSSION OF TWO CASES OF TETRYL DERMATITIS

DR. S. W. BECKER: I had the opportunity to attend a course on industrial dermatoses given by Dr. Schwartz last summer in Washington. We visited some of the munition plants and saw tetryl being manufactured and used. The difficulty in treatment is obvious. The dermatitis is due to sensitization to a chemical, and hypersensitivity cannot be decreased by injection as can sensitization to poison ivy or ragweed. Unless the patient's skin can be treated by some local application, the only alternative procedure is to take the patient away from this kind of work, provided he does not become "hardened." Tetryl is related to TNT, which is a nitrate compound with a tendency to produce sensitization. A rather large percentage of patients who work with tetryl acquire dermatitis of the face; those working with TNT usually acquire dermatitis of the hands.

DR. L. F. WEBER: I have had occasion to see a few patients with tetryl dermatitis in one large plant near Chicago. I think the members of the medical department of the plant are familiar with tetryl dermatitis and do not expect to decrease its incidence. They are more interested in dermatologic conditions other than tetryl dermatitis. It is a question of differentiating a good many of the vesicular eruptions of the extremities and other dermatoses. I think that the eruption as demonstrated here by Dr. Mitchell is typical. Most persons who work with tetryl have a yellow staining of the hands. That does not mean that all of them are going to have a tetryl dermatitis. In the majority of those who acquire a tetryl dermatitis, it develops within six or eight days, but in some it develops later, after as much as twenty days. The question comes up what to do with these patients that acquire tetryl dermatitis. If they stop work, they usually improve. Some of them are then put back to work on the same job. If there is a recurrence, it means definite removal of the patient from his former occupation. Many of the workers in this particular plant became so sensitive that they were unable to work in the area. To come into contact with a worker with tetryl dust on his clothing would be sufficient to bring about a recurrence of their dermatitis.

One other thing that interested me was the question of patch tests with tetryl. I have had occasion to make some patch tests with the material, and if I had to do it over again I should not have made those tests. I shall make no tests in the future.

DR. S. ROTHMAN: In the first World War I saw a couple of soldiers who with intent to malinger took picric acid (trinitrophenol) internally. They wanted to simulate jaundice. Their palms showed an orange-yellow discoloration of intense degree. I should like to ask Dr. Mitchell if the orange-yellow discoloration in the palms of his patients is due to picric acid.

DR. UDO J. WILE, Ann Arbor, Mich.: Is the yellow discoloration which we saw on the palms also seen on the soles?

DR. J. H. MITCHELL: No.

DR. CLEVELAND J. WHITE: I think one of these cases shows clearly what protective clothing will do, for the area covered by the patient's hat shows neither dermatitis nor pigmentation. This is an extremely interesting and a typical case of sensitivity to tetryl.

DR. MAURICE OPPENHEIM (by invitation): I want to cite my experience in the first World War. Tetryl was not used in the first World War by the American Army, so far as I know. TNT and picric acid compound were used. TNT causes a dermatitis like that produced by poison ivy. Picric acid dermatitis involves the face and discolors the hair, nails, palms and soles yellow. I think it may be that picric acid or picrate is eliminated by the skin and does not enter by the respiratory tract. TNT dermatitis is characterized by cutaneous symptoms, as are other manifestations of hypersensitization, such as dermatitis from poison ivy, primroses, etc. I was present when Dr. Louis Schwartz delivered a lecture on dermatitis caused by tetryl. I was impressed with the pictures he showed. In almost all cases there were lesions on the skin of the face but none on the hands. That was peculiar, because contact dermatitis caused by hypersensitivity should appear on the hands too.

DR. J. H. MITCHELL: Early in World War I, picric acid was used as a means of producing simulated icterus. The French promptly developed tests for the chemical, and the practice ceased.

Tetryl was used extensively in the first World War, notwithstanding the statement just made by Dr. Oppenheim. A number of valuable contributions appeared in the English medical journals in 1915 and 1916, and there appears in Dr. Oppenheim's work a reference by Koelsch to tetryl dermatitis (Ullmann, K.; Oppenheim, M., and Rille, J. H.: Die Schädigungen der Haut durch Beruf und gewerbliche Arbeit, Leipzig, Leopold Voss, vol. 2, pts. 5 to 8, p. 325).

The problem of tetryl dermatitis is complicated. I was asked last December to visit the plant. The members are probably familiar with the construction of munitions plants. Regulations require that buildings must be small and widely separated one from the other. They are what Dr. O'Leary has just referred to as "glorified outhouses." This plant went into production early in December. Apparently no one was aware of the serious consequence of tetryl dermatitis. The British, having had much experience with it, devised some rules which I incorporated into recommendations I made to the firm after visiting the plant. In the course of processing, tetryl becomes so finely pulverized that the dust is not visible. This dust permeates the entire establishment, and the workers' hair, skin and clothing become stained a bright canary yellow. The tables and benches where the workers have their lunch are also stained yellow.

Tetryl is soluble in water only to 0.007 per cent. It is slightly more soluble in alcohol and oil but is freely soluble in acetone and benzene. The problems involved in the prevention of tetryl dermatitis are many. First, every applicant for work should be given patch tests with a suspension and solution of tetryl in olive oil. After trying out many patch tests, I found that this was the most reliable type. Workers should be examined every day for any sign of dermatitis. Each worker should have two lockers, one to contain the street clothing and the other to contain the work clothing. Each worker should be supplied with a suit with anklets and wristlets and fitting close around the neck. He should also be provided with a mask. The suits should be washed frequently, and the workers should have leather gloves which can be washed. At the end of the day the workers should be required to take a shower and put on the street clothing, which has not been in contact with the work clothing. The work rooms should be so arranged that they can be washed down daily with a stream of water. Each work bench should be supplied with a device for producing a forced draft and containing a grill, beneath which is wet coke to take up the dust and to reduce fire hazards.

Apparently sunlight has no effect on the production of the dermatitis. Light causes the chemical to change from a pale yellow to a deep orange, as I demonstrated in the exhibit here presented after exposure to ultraviolet radiation from a quartz lamp. A similar result is produced by exposure to light of fabric saturated with an acetone solution of tetryl. I have been able to demonstrate that the canary yellow staining of the palms is due to the affinity of the corneous layers of the epidermis for the chemical and that it has no bearing on exposure to light. Application of the olive oil solution will stain my heels as promptly and as effectively as it stains my palms, but application of the test solutions to the flexor surface of my forearm and to the inner surface of the upper part of my arm will cause neither the slightest staining nor any suggestion of dermatitis.

Incidence of sensitivity varies in different reports from 23 to 40 per cent. Complexion appears to have little influence on the development of dermatitis. Seborrhea, however, is an important factor, as it has been pointed out that tetryl is soluble in oil. This accounts for the relative immunity of the hands as compared with the face.

Involvement of the genitalia is of no importance as far as has been observed in this plant and as far as could be learned from perusal of the literature.

Toxic systemic disturbances have no importance whatsoever, as far as can be learned from the reports in the literature. Intensive laboratory examinations of the workers in this group corroborate this statement. English reports noted much loss of hair in some cases, but I have found no evidence of this in the short time these workers have been under my observation.

So-Called Myoblastoma. Presented by DR. M. H. EBERT and (by invitation) DR. A. H. SLEPYAN.

About five years ago, this 13 year old Negro boy noticed a small nodule on the dorsum of the left hand, in the webbed area between the thumb and index finger. Since then there has been a slow but gradual increase in the number and size of these small nodules. They occasioned no sensation except on catching a ball.

When first seen three weeks ago, there was an irregular tumor mass of the size of a quarter, made up of confluent, pea-sized nodules.

The tumor was freely movable over the subcutaneous tissue but adherent to the overlying skin. The lesion was irregularly firm and of the consistency of a hard rubber ball. The surface of the lesion imparted a yellowish hue.

A roentgenogram of the hand revealed no osseous involvement.

The past history is essentially normal, except for defective eyesight in the left eye, due to detachment of the retina.

Histologic Picture.—The tumor mass was located in the lower two thirds of the corium and extended as deep as the section taken for biopsy. It was encapsulated by connective tissue, but there were a few satellite islands of tumor tissue, some of which were in close approximation to sweat ducts and sweat glands. In one section a sweat duct penetrated directly into the tumor. The tumor cells were large and round or oval, with a small light-staining nucleus, usually eccentric. The cytoplasm was filled with small amorphous, acidophilic granules. The cell boundaries were difficult to make out. Many groups were evidently syncytial. There was no evidence of striation. Cell groups were arranged in strands about a central syncytial mass, and these strands and groups were separated by connective tissue.

DISCUSSION

DR. FREDERICK R. SCHMIDT: Clinically this little tumor resembles the three that I presented some time ago. When the sections are first studied under the microscope, the impression is that it is an adenoma of a sweat gland, especially in the specimen submitted today, where there is encapsulation by connective tissue, so that it stands out as a small globular complex. That was the impression of Abrikossoff (Abrikossoff, A. I.: Ueber Myoma ausgehend von der quergestreiften willkürlichen Muskulatur, *Virchows Arch. f. path. Anat.* **260**: 215, 1926) who first presented these tumors in 1926. He thought that they were a form of embryonal rest in the skin, coming to full expression in adult life. On further study I was struck by the fact that the individual cells, containing granules and eccentric, pyknotic nuclei, are separated one from another by a syncytium. Some of the cells appear to be directly derived from older cells, and such a degeneration, of course, is not in line with an embryonal rest or hamartoma. The origin of the granules is obscure, and I know that Drs. Ebert and Slepyan will use many different stains in an effort to determine their genesis.

DR. UDO J. WILE, Ann Arbor, Mich.: Does any one know whether Dr. Montgomery has any such tumors in his collection?

DR. PAUL O'LEARY, Rochester, Minn.: Not that I know of.

DR. S. W. BECKER: Some time ago Dr. Clarence Shaw, of Chattanooga, Tenn., sent me a specimen of one of these tumors which was in a portion of the body, the upper part of the chest, where the platysma myoides muscle is located. The opinion is that it is a tumor of the striped muscle. I cannot conceive of striped muscle being present in this particular location. I wonder whether Dr. Ebert has any ideas on that subject.

DR. M. R. CARO: I think that this is a benign tumor of muscle cells that are so immature that they have not yet been differentiated into either smooth or striped muscle.

DR. M. H. EBERT: I do not suppose that these little tumors are of great practical importance, but they are interesting because of the unusual cells and the theories involved to explain their origin. I wish to express my appreciation to Dr. Frederick Schmidt for demonstrating to this society the first microscopic section of this tumor and for his informative article on the subject in the August 1942 issue of the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY.

When Dr. Slepyan and I first saw this patient we thought of various possible diagnoses: sebaceous gland tumor, fibroma and xanthoma. We were surprised when the sections came through. I believe Dr. Caro was the first to recognize the tumor as a myoblastoma.

The first series of 5 cases were reported in *Virchow's Archiv für pathologische Anatomie und Physiologie und für klinische Medicin* by Abrikossoff, of Moscow. Since the majority were found in the tongue and seemed to resemble embryonic striped muscle cells, as described by a Russian histologist, Goellewski (*Arch. f. mikr. Anat.* **60**:111, 1902), he called the tumor a myoblastoma, a new growth stimulated by irritation of the striped muscle which tended to reproduce the embryonic type of cell.

The next important paper was written by Klinge, who elaborated a much more complicated theory as to its origin. In the embryo the primordial striped muscle cells and connective tissue cells are grouped along the spinal column in the myotomes. Later the connective tissue cells migrate to the cutis, while the embryonic muscle cells still remain in the myotome. Klinge explained the presence of myoblasts in the skin or mucosa by assuming an improper separation of these two types of cell in the myotome during embryonic development. Some myoblasts have migrated with the connective tissue cells to the periphery.

Gray and Greenfeld (*Am. J. Cancer* **30**:699, 1937) took exception to this theory of origin based on Goellewski's description of primordial striped muscle cells. They cited later work by Zeichel (*Ztschr. f. d. ges. Anat.* **74**:593, 1924) and several others, who did not find granular polyhedral cells in the primitive muscle that might be compared with the tumor cells of the "so-called myoblastoma." Gray and Greenfeld expressed the belief that Klinge's theory was not founded on fact and that the origin of the peculiar granular tumor cell must be determined if possible in each individual case by evidences of transition from other types of cell in or near the tumor. They considered the term "myoblastoma" untenable. In instances when the tumor is found in the tongue, the striped muscle is the likely origin. In our case today the sweat glands or ducts may be a possible source. Sweat ducts are seen entering directly into the tumor mass. The microchemistry of the granules is still unknown. Dr. Finnerud suggested that the cells resembled those of xanthoma. Studies made in other laboratories have shown that there is no relationship to xanthoma.

DR. M. R. CARO: I examined sections from this specimen stained with sudan III, and there was no fat present.

Chronic Recurring Lichen Planus. Presented by DR. JAMES MITCHELL and (by invitation) DR. RALPH H. SCULL.

A. K., a white man aged 54, was admitted to the outpatient department of Rush Medical College four years ago, complaining of an itching, erythematous maculopapular eruption, most pronounced on the arms and legs. He stated that this came on suddenly at the time of a serious illness of his present wife.

He had a similar attack fourteen years ago, following the death of his first wife. He was treated at Rush Medical College for lichen planus and was discharged after six months.

Examination showed angular and round, pinhead-sized to pea-sized, red to bluish red maculopapular lesions on the upper and lower extremities, with a few distributed over the trunk. The buccal mucosa showed a number of adherent white plaques.

The Wassermann and Kahn reactions were negative.

The eruption was again diagnosed as lichen planus and treated with bismuth subsalicylate intramuscularly and later with mercury intramuscularly and by mouth, with little response. After consultation, iodobismitol with benzocaine was given, and nearly all the lesions disappeared, save a few on the legs that were treated with roentgen therapy.

A few weeks later the lesions returned; they were less angular and were covered with silvery scales. The eruption has not responded to any measures except ultraviolet irradiation and roentgen therapy. In a few weeks the lesions return.

Histologic examination of tissue from a lesion of the right thigh showed hyperkeratosis, hypertrophy of the stratum granulosum and acanthosis. There was no sharp line of demarcation between the epidermis and the infiltrate in the cutis, which was composed of lymphocytes and connective tissue cells (fig. 1).

DISCUSSION

DR. RICHARD WEISS, St. Louis: The eruption, while it showed a few lichenoid papules on the arms, seemed to be more of a dermatitis. I was wondering whether there was a metallic element in it, whether arsenic or bismuth had anything to do with it. The lesions

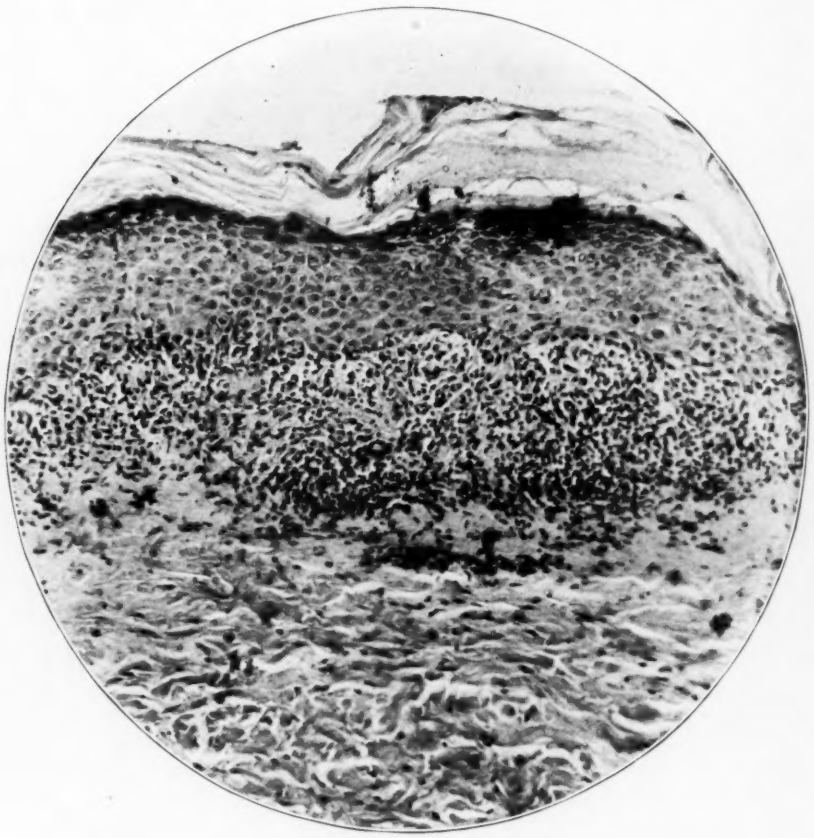

Fig. 1.—Photomicrograph of a section from a lesion of recurring lichen planus.

in the mouth were rather pronounced and at this time looked to me more like leukoplakia than lichen planus. I think a diagnosis of lichen planus could not be made on this single examination.

DR. UDO J. WILE, Ann Arbor, Mich.: Was there not a certain degree of mild atrophy on the skin of the forearm? It seemed to me that the forearm, from the elbow to the wrist, of both arms seemed slightly atrophic, though there were lesions of a lichenoid character present.

DR. C. W. FINNERUD: I cannot disagree with the diagnosis clinically. Like Dr. Weiss, I might have disagreement with it from what I saw on the forearms rather than from the oral lesions. Without reading the history, I considered the lesions in the mouth those of lichen planus. The sections presented under the microscope I am sure make the diagnosis definite.

DR. S. RATHMAN: Seeing the sharply demarcated acute dermatitis on the extremities, I asked the patient whether he had had any irradiation therapy. He said that he had. The picture as it presents itself today is compatible with lichen planus influenced by therapy. I thought the oral lesions were typical of lichen planus.

DR. JAMES H. MITCHELL: Dr. Scull just recently asked me to see this patient, because he had had him under observation for some time at different periods in the night clinic, which I do not attend. Dr. Scull is conservative in his clinical observations. He was in doubt about the possibility of this being lichen planus because of the failure to respond to treatment at this time. After considerable talk with the patient I learned from the history that Dr. Ormsby had demonstrated him when Dr. MacLeod was here and had made a diagnosis of lichen planus. He remembered all the details, even his clinic number nineteen years ago. The number given was checked and found to be correct.

I gave Dr. Scull my moral support, that is all. I believe the disease is lichen planus in all the areas, some of which have been changed in appearance by treatment. I suggested that Dr. Scull perform a biopsy, and the result is as presented.

DR. RALPH H. SCULL (by invitation): I considered this case interesting first because the attacks were associated with mental shock; secondly, because of the lack of response to treatment, and, lastly, because of the change in the character of the lesions from angular shiny-topped maculopapules to round and oval scaly ones.

A Case for Diagnosis (Granuloma Inguinale? Lymphogranuloma Venereum? Tuberculosis?). Presented by DR. EDWARD A. OLIVER.

H. M., a Negro aged 45, states that the present ulceration began in July 1919, when there developed on the back and sides of the neck and on the sternum swellings which broke down and ulcerated. Shortly after the appearance of those lesions, he noticed a lump in the groin on the inner aspect of the left thigh. This broke down and ulcerated and has remained open ever since. The Wassermann reaction was positive. Tuberculin tests elicited positive reactions, but a roentgenogram of the chest showed both pulmonary fields clear. No tubercle bacilli were found in the sputum. The Frei reactions were positive.

The pathologist at the Veterans' Administration Facility at Hines, Ill., reported that sections from the edge of the lesion showed only chronic inflammation. No Donovan bodies were found, but in 1938 the patient received fifteen injections of antimony thioglycollamide and the lesion improved considerably.

DISCUSSION

DR. HERBERT RATTNER: I thought that the inguinal lesion clinically was granuloma inguinale, in spite of the fact that the Donovan bodies could not be found. The positive Frei reactions might indicate the presence also of lymphogranuloma venereum.

DR. UDO J. WILE, Ann Arbor, Mich.: Is it possible for the patient to have two kinds of lesions? The lesions on the neck and axilla certainly did not look like the lesion in the groin. The former suggested to me that he might have two different diseases. The neck and axillary lesions were like those seen in hidradenitis.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: I agree with Doctor Wile's suggestion that this may be a form of pyoderma, particularly hidradenitis suppurativa. In addition to the extensive ulceration of the groin, there is infection of the skin of the back of the neck with small sausages of infiltrated sinus tracts and also scars of other healed lesions on the sternum and in the axillas. The best treatment to the groin will be complete excision of the infected site, perhaps to be followed by grafts; but, first of all, there should be a period of cleansing treatment including the use of filtered roentgen rays and sulfonamide compounds. In some such cases when the skin is excessively oily and there are widespread pyogenic foci in the selected sites, I have noted improvement from the use of estrogenic substance in patients of both sexes.

DR. EDWARD A. OLIVER: I saw this patient last week for the first time. The question of diagnosis brings up three possibilities: granuloma inguinale, lymphogranuloma venereum and possibly tuberculosis.

Pityriasis Rubra Pilaris. Presented by DR. FRANCIS E. SENEAR.

P. W., a man aged 48, first noticed scaling and roughness of the dorsa of the proximal phalanges of his fingers about eight years ago. A few months later scaling of his face developed and his fingers became stiff, owing to thickening of the palms. Later a diffuse redness of the trunk, upper extremities and face developed. The scalp became heavily crusted.

On his admission to the hospital, on Dec. 24, 1942, there was a generalized erythroderma except for small areas on the thighs, forearms and abdomen which presented numerous discrete pinhead-sized acuminate horny follicular papules separated by uninvolved skin. These patches were severely symmetric in distribution. The face was yellowish red and waxy. The scalp was thickened and covered with heavy whitish scales. Plugged follicles were present on the dorsa of the proximal phalanges of the fingers. The palms and soles were greatly thickened, waxy, yellowish and deeply fissured. The nails were thickened and deformed. The histologic picture was typical of pityriasis rubra pilaris.

The basal metabolism rate was —3 per cent on one occasion and +5 per cent on another. The patient has been treated with 300,000 U. S. P. units of vitamin A daily, with some improvement in the condition of the skin.

DISCUSSION

Dr. Paul A. O'Leary, Rochester, Minn.: Recently we have had 2 patients with pityriasis rubra pilaris, in both of whom the cutaneous lesions disappeared with vitamin A therapy. One was a girl 3 years old, and the other was a man 52 years of age, who, by the way, had a visual acuity better than average. Not all patients with vitamin A deficiencies have delayed light adaptation; hence this test cannot be used as an indicator of avitaminosis A. One other point is that patients who have a carotenemia may also have evidence of night blindness and vitamin A deficiency.

Dr. Udo J. Wile, Ann Arbor, Mich.: I have had an instructive experience with pityriasis rubra pilaris because I think I used to miss a good many cases largely because of the rigid criteria required for such a diagnosis. I am impressed with the fact that in most of the cases of pityriasis rubra pilaris the manifestations do not agree with the textbook picture. The case today is a happy illustration because the observations are typical. I have had cases in which the diagnosis of pityriasis rubra pilaris was ultimately decided by others who observed the patients with me. In some of the cases for a long time there were no vesicular lesions, and in some the patient's face and head were not involved. My colleagues and I have had a fairly large number of such patients under observation. Dr. Curtis did considerable work on vitamin therapy previous to his association with me, and I wonder if he would say something.

Dr. Arthur Curtis, Ann Arbor, Mich.: During the past year I have had the opportunity of determining the vitamin A blood levels of 3 patients with pityriasis rubra pilaris. In these the levels of vitamin A have been about half as high as normal, which confirms the biophotometric observation of Dr. L. A. Brunsting in this disease. In experimental animals it has been found that a normal blood level of vitamin A is maintained as long as adequate stores remain in the liver. Once the liver stores are depleted, the vitamin A level falls rapidly. It is interesting to speculate why patients with pityriasis rubra pilaris have a reduced vitamin A blood level. Many of them have an adequate intake of carotene. Whether they are unable to convert carotene to vitamin A, whether the individual requirements are greater in this disease, whether the patients are unable to store vitamin A or absorb it or whether they lose it are questions which are unanswered at the present time.

Dr. Udo J. Wile: This patient has been treated with 300,000 U. S. P. units of vitamin A daily, with some improvement in the general condition and in the condition of the skin.

Dr. Theodore Cornbleet: There is a question of what happens to the vitamin A. It has been my feeling that vitamin A deficiency is not the only factor in pityriasis rubra pilaris, because patients with the disease do not seem to get well and stay well when the vitamin A level is brought up to normal and use of a normal diet is continued, as one would expect under ordinary conditions. There may be some central condition which disrupts their vitamin A level more than that of a normal person. The liver would be the natural organ to study, but, unfortunately, specimens of liver cannot be taken from these patients for biopsy. In a recent study I showed that the skin itself does not contain any vitamin A but that the fat and subcutaneous tissues do, and it would be worth while to perform biopsies at intervals on patients with pityriasis rubra pilaris to see whether there is an actual deficiency in the tissues. What is in the circulating blood does not reflect what is in the fixed tissue. By such a process one could find what there is in the tissues of persons with this disease.

Pityriasis rubra pilaris is not an avitaminosis in the ordinary sense. The patients require too much material for an ordinary deficiency, and this enormous dosage induces partial restitution. This improvement, furthermore, is quickly lost without continued therapy. The most plausible explanation offered is that the liver fails to convert carotene to vitamin A to the extent it should.

DR. JAMES H. MITCHELL: In connection with Dr. O'Leary's statement, I saw a woman of 35, a serious-minded person, who assured me that she would never be obliged to wear glasses because she was taking large doses of vitamin A.

A Case for Diagnosis (Vascular Disease?). Presented by DR. EDWARD A. OLIVER and (by invitation) DR. S. M. BLUEFARB.

R. R., a man aged 41, was first seen at the dermatologic department of Northwestern University Medical School on Jan. 11, 1943, complaining of pain in both feet. He states that about two hours seems to be the limit of his endurance in an upright posture. After this length of time he must sit down. This condition has been gradually developing for the past four years. An ulcer on the lateral aspect of the left ankle has been present since November 1939. His feet are so painful that it is impossible for him to do any work while standing. His ankles are swollen during the day, but this swelling disappears at night. Early in the morning he experiences "cramps" in his legs.

Bilateral cataracts were removed in 1936. He drinks about 1 pint (475 cc.) of liquor per week. One brother has epilepsy.

Physical examination reveals a man who appears to be much older than his age indicates. The skin is ichthyotic. The genitalia are infantile, with feminine distribution of hair. The liver is palpable 3 cm. below the costal margin. The spleen is not palpable. The skin of the lower extremities shows atrophic changes, with ulceration on the lateral aspect of the left ankle. There is absence of the subcutaneous fat from the foot and the lower part of the legs and evidence of muscular atrophy. The blood pressure is 150 systolic and 80 diastolic.

Urinalysis gave values within essentially normal limits. The Kahn and Wassermann reactions of the blood were negative. Examination of the blood showed 5,020,000 erythrocytes, a hemoglobin content of 15.6 Gm. and 8,150 leukocytes.

The neurologic diagnosis was alcoholic polyneuritis with trophic changes in the lower extremities.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis, Minn.: The late Professor Bloch reported a study on a patient similar to this before the Washington meeting of the American Dermatological Association a number of years ago, and the paper was later published in the ARCHIVES. He brought out the fact that this change, whether it was due to endocrine imbalance or not, was a poikiloderma-like change. When I saw this patient, I remembered that paper, and I could see the possibility of a poikiloderma-like change in the extremities.

DR. S. M. BLUEFARB (by invitation): We are not quite sure of the exact diagnosis, but the condition is probably on a peripheral vascular basis. I believe another interesting feature is the rapid aging of this man. Here is a man who looks much older than his age would indicate: He has gray hair, and he has had surgical removal of bilateral cataracts. Associated with this rapid process of aging, he has an infantile sexual organ. This brings up the question of rapid aging due to a decline in the sexual endocrine glands, with a loss of sexual powers.

DR. UDO J. WILE, Ann Arbor, Mich.: I should like to ask Dr. Bluefarb whether there are any changes in this man's superficial reflexes.

DR. S. M. BLUEFARB: A thorough neurologic examination was made, and the results were completely normal. There were no pathologic reflexes present.

DR. UDO J. WILE: The amount of alcohol this man has consumed suggests polyneuritis as an etiologic factor.

DR. S. M. BLUEFARB: It was the opinion of the neurologist that the disease was an alcoholic polyneuritis and that the changes in the skin were secondary to the polyneuritis. However, we were not satisfied with the diagnosis, and it was our impression that the condition was due to an underlying vascular process.

Mycosis Fungoides. Presented by DR. JAMES H. MITCHELL and (by invitation) DR. RALPH H. SCULL.

E. J., a Negro aged 42, presents an eruption which began in May 1942 after an injection of tetanus antitoxin. At this time he experienced a generalized itching associated with what he describes as swollen plaques over the entire body. He received some medical treatment before coming to this institution. He had never had any disease of the skin prior to this.

Examination shows a generalized lichenification and hyperpigmentation of the skin, with superimposed plaques of various configurations and lighter than the surrounding skin.

The Wassermann and Kahn reactions were negative. The blood showed 36 per cent eosinophils.

Histologic examination of the tissue showed acanthosis of the epithelium and a polymorphous infiltrate of the upper part of the corium composed of lymphocytes and giant lymphocytes, connective tissue cells and multinuclear cells (figs. 2 and 3).

DISCUSSION

DR. UDO J. WILE, Ann Arbor, Mich.: Has any member ever seen mycosis fungoides in a Negro? I cannot recall having seen one with the disease.

DR. RICHARD WEISS, St. Louis: The rather curious feature of mycosis fungoides as it appears in a Negro is the bizarre type of lesion that is present. A Negro does not, as a

Fig. 2.—Photomicrograph of a section from a lesion of mycosis fungoides in a Negro (low power).

rule, present the cleancut plaque type of lesion that one encounters so often in a white person. The lesions are more bizarre, and when one first sees them one does not think of mycosis fungoides until they have been examined closely.

DR. UDO J. WILE: Perhaps the reason I did not recall having seen the disease in a Negro is that there are few members of that race in Ann Arbor. The Negro population is less than 2 per cent of the total.

DR. LOUIS A. BRUNTING, Rochester, Minn.: The evidence for mycosis fungoides in this patient rests largely on the interpretation of the biopsy specimen. In this case there is a widespread, symmetric eruption with an eczematoid quality, a pale zone of normal skin around the nose and mouth, alopecia of the outer part of the eyebrows and white dermographism. It has been my experience that in patients with disseminated neurodermatitis the microscopic

picture of the skin may resemble that of mycosis fungoides owing perhaps to the stimulation of the cells of the reticuloendothelial system, and it sometimes requires a period of observation of months or even several years in order to decide the question. For this patient I should favor the diagnosis of neurodermatitis or atopic dermatitis.

DR. M. R. CARO: There are a number of features in this case which call to my mind a group of cases described by Sulzberger and Garbe as "exudative discoid and lichenoid chronic dermatosis" (ARCH. DERMAT. & SYPH. **36**:247 [Aug.] 1937). In this case the involvement of the forehead and the genitalia, the intense itching, the follicular lesions and other features suggest that the patient should be studied with that possible diagnosis in mind.

DR. UDO J. WILE: I am not qualified to discuss mycosis fungoides in the Negro and therefore will accept any diagnosis which is made. However, there is one point in connection

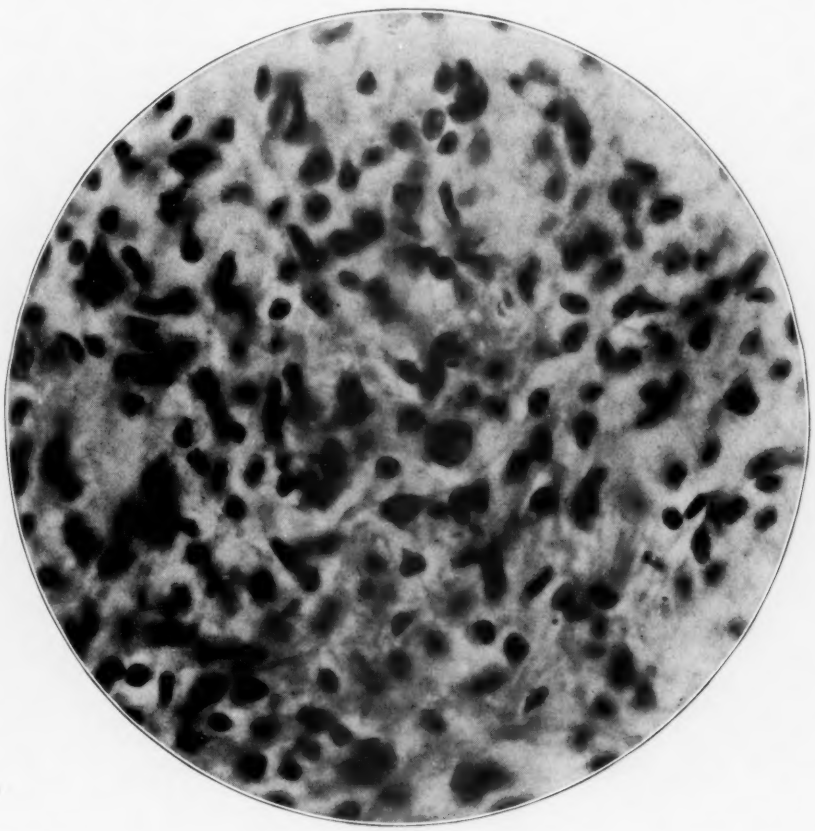

Fig. 3.—Photomicrograph of a section from a lesion of mycosis fungoides in a Negro (high power).

with the physical observations which is unusual. In most cases of mycosis fungoides there is little if any involvement of the lymph glands. This patient had extensive lymphadenopathy and some enlargement of the spleen. These observations are rather paradoxic, for, although it was once believed that mycosis fungoides originates in the lymph glands, it is now believed that involvement of the lymph glands is relatively slight and in many cases does not occur at all.

DR. JAMES H. MITCHELL: I saw this patient only once and suggested that a biopsy be made. Dr. Scull gave me the sections yesterday afternoon for photographing. I had to work rapidly and did not have time to study them. I agree with Dr. Scull that the findings are sufficient to lead to the diagnosis of mycosis fungoides, but it may be necessary to change the diagnosis.

Lupus Erythematosus of the Lips. Presented by DR. MICHAEL H. EBERT.

This 54 year old Negro, C. J., was first seen in our clinic in July 1942, with a heavy pyogenic crusting of the lips and bleeding areas at the borders of the crusts. The borders of the lesions themselves were sharply demarcated, as seen at present. These lesions had been present since January 1942. No other lesions have been present at any time. The lesions were soaked in aluminum subacetate and 5 per cent boric acid ointment was applied; good results were obtained on the secondary infection.

The patient disappeared from August to late December, at which time there was no discomfort of his lips. He now returns, with moderate fissuring of the lesion of the lower lip.

The results observed at the physical examination were essentially normal except for the lesions of the lips. Laboratory data, including results of a hematologic examination and a roentgenogram of the chest, were normal.

DISCUSSION

DR. C. W. FINNERUD: I do not think any one will differ with the diagnosis. I was interested in the fact that in spite of the lesions of the vermilion border there was no change in the mucous membranes of the mouth. Often in patients with extensive involvement of the vermilion border one will find lesions in the mouth.

Book Reviews

A Handbook of Allergy for Students and Practitioners. By Wyndham B. Blanton, M.A., M.D., Litt.D., Professor of Clinical Medicine, Medical College of Virginia, Richmond, Va. Price, $3.00. Pp. 190, with 20 black and white illustrations. Springfield, Ill.: Charles C Thomas, Publisher, 1942.

In a compact volume, the author has given a large amount of information which is readable and easily understood. The subject is divided into three main headings: the fundamentals, the causes and the results of allergy: Part III discusses the results of allergy and includes chapters on allergy of the nose and throat, asthma, dermatologic allergy and gastrointestinal and other allergies.

The subject of dermatologic allergy occupies 20 pages, and the opinions expressed should meet with the approval of most dermatologists. A minor criticism would be the inclusion of the luetin and the leprin test in a list of routine tests "daily applied" in the diagnosis of infectious diseases. Few dermatologists use the luetin test at present, and the leprin (more often called lepromin) test is not diagnostic of leprosy. It is only a prognostic test. In this chapter the word pruritus is also consistently misspelled.

The value of the book as a whole is increased by a reasonable number of photographs, charts and tables. Short paragraphs on history appear in each chapter; these give the names of investigators who are thought to have contributed most to the knowledge of the subject.

A useful appendix of 30 pages is added, in which diets free from egg, wheat and milk are given and numerous recipes which do not contain these important foods.

In discussing the subject of seasonal inhalant allergy (pollen allergy) the author includes botanic information about trees, grasses and weeds. His knowledge of this subject is not questioned, but it is unfortunate that an obvious mistake was made on page 78 in the caption of an illustration of one of the rhus plants. The drawing in question is labeled Rhus toxicodendron diversiloba. It protrays several compound leaves with seven oval leaflets. This would be a fair illustration of the poison sumach, but certainly not of Rhus diversiloba (poison oak), which always has three leaflets.

The book is recommended to students and physicians, including dermatologists.

Synopsis of Diseases of the Skin. By Richard L. Sutton Sr., M.D., Emeritus Professor of Dermatology, University of Kansas Medical School, and Richard L. Sutton Jr., M.D., Assistant Professor of Dermatology, University of Kansas Medical School. Price, $5.00. Pp. 475, with 413 illustrations. St. Louis: The C. V. Mosby Company, 1943.

For medical students, for nurses—and even for dermatologists as a quick, concise reference work—this book is of value. Grouping of the contents on an etiologic basis helps the student to obtain a general understanding of diseases of the skin and provides the teacher with a systematic outline which can be easily followed. There are hundreds of bibliographic references scattered through the text. The more common the disease, the greater is the amount of space devoted to its discussion. Rare diseases, if mentioned at all are but briefly considered.

The authors have followed the "Standard Nomenclature of Disease," omitting synonyms and eponyms in most instances. However, it is difficult to understand why such terms as "lymphogranuloma inguinale" and "lymphopathia venerea" should be used. The effort to rescue the term "eczema" from "the trash heap" of dermatology, while not entirely successful, is commendable and will be a help to all readers.

Syphilis is briefly considered, with an up-to-date résumé of treatment and many references. In this book much has been said in few words.

Essentials of Syphilology. By Rudolph H. Kampmeier, Associate Professor of Medicine, Vanderbilt University School of Medicine; in Charge of the Syphilis Clinic and Visiting Physician to Vanderbilt University Hospital. Price, $5.00. Pp. 516, with 87 illustrations. Philadelphia: J. B. Lippincott Company, 1943.

The author presents more than the essentials of syphilology, which the title of his book implies. A great deal of information is crowded into this little volume. No effort is made at originality, and no new concepts are offered. The author cites numerous authorities, mostly American, and expresses his own opinion in many instances. The illustrations are excellent, especially those of secondary syphilis taken from material in the Vanderbilt University Hospital. The book is primarily intended for the student and general practitioner, who has little

knowledge of syphilis in its various manifestations; however, a great deal in the text will be of interest to the specialist. It is obvious that in a book of 516 pages, the subject of syphilis cannot be covered in an adequate manner. Owing to this brevity, criticisms arise, and some of the subjects create divergent opinions. However, there are excellent references on such controversial matters for the reader.

The book has nineteen chapters, each with numerous subdivisions and appended historical notes, including chapters on sociologic studies in the prevention and control of this disease.

The author lays great stress on the diagnosis of early syphilis, especially on dark field examination. This method is not described in detail, because the author does not consider the procedure within the domain of the general practitioner; such an examination should be made by a qualified expert. The author rightly states that the day has passed when the diagnosis of secondary syphilis can be justified without confirmation by dark field examination or blood tests positive for syphilis.

The book is compact, is well printed on excellent paper and is well bound; it supplies the main points needed by the general practitioner in the study of syphilis.

The 1942 Year Book of Dermatology and Syphilology. By Fred Wise, M.D., and Marion B. Sulzberger, M.D. Price, $3.00. Pp. 664, with 91 illustrations. Chicago: The Year Book Publishers, Inc., 1943.

The high character of the "Year Book of Dermatology and Syphilology" is maintained in the present volume. The 494 important contributions relating to dermatology and syphilology of the past year have been abstracted from ninety-four journals published in eleven countries. The articles are grouped into fourteen chapters according to subjects, such as mycotic infection, drug eruptions, cancer, syphilis and other venereal diseases, therapy and experimental studies. One of the most valuable features is the personal comment by the authors on 146 of the articles which have been abstracted.

Special attention has been paid to publications relating to the war effort. Seven topics mentioned in the previous edition as being of special interest in wartime have been stressed in the present volume.

An original contribution is given by the authors on the important subject of burns. Other subjects include the treatment of frozen skin and tissue, methods of preventing industrial diseases of the skin, a new remedy for scabies, cutaneous hazards in airplane factories and tropical diseases of the skin.

In line with the trend of the radio for questions and answers, twenty rather difficult questions on up-to-date subjects are included on the dust jacket.

The illustrations are well chosen, and, in spite of being presented on rather thin paper, have been well reproduced.

The volume should prove to be an invaluable addition to the library of every dermatologist.

Essentials of Industrial Health. By C. O. Sappington, M.D., Dr. P.H., Consulting Industrial Hygienist; President, Central States Society of Industrial Medicine and Surgery. Price, $6.50. Pp. 626, with 53 text illustrations. Philadelphia: J. B. Lippincott Company, 1943.

This book is a complete factual compilation on industrial medicine which should be of extreme value to both the medical and the nonmedical personnel interested in this subject. The material is compactly presented and is ideal for reference.

It covers not only medicine and surgery but subjects of interest to the industrial hygienist, health administrator, engineer, plant supervisor and all persons engaged in the prevention of industrial disease and accidents.

The author is a well recognized authority in the medical, chemical engineering and medicolegal aspects of this subject. Physicians intending to make industrial medicine or industrial surgery their chosen specialty will profit by his experience.

Since it was not the intention of the author to go into detail on every phase of industrial health, the reviewer must admit that his treatment of industrial dermatoses is well done, because it helps, at least, to give the background on which the actual dermatitis develops and the agents producing the eruption. The subject mattter has been arranged according to occupations, so as to facilitate the search for the various irritants contacted.

All this makes this volume an excellent reference book for the dermatologist, especially if he is interested in industrial diseases of the skin. For the size of the book, a remarkable amount of information is supplied.